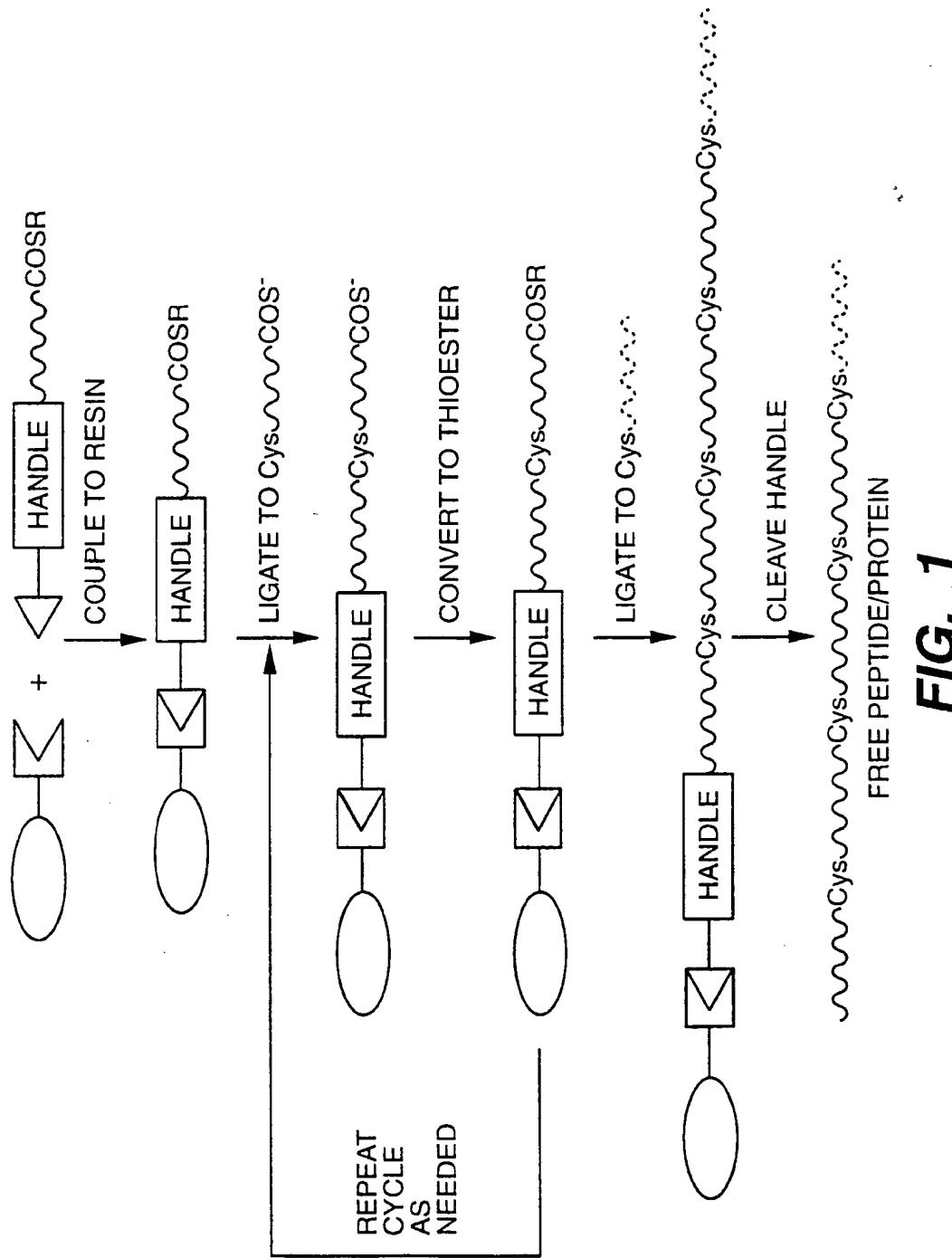
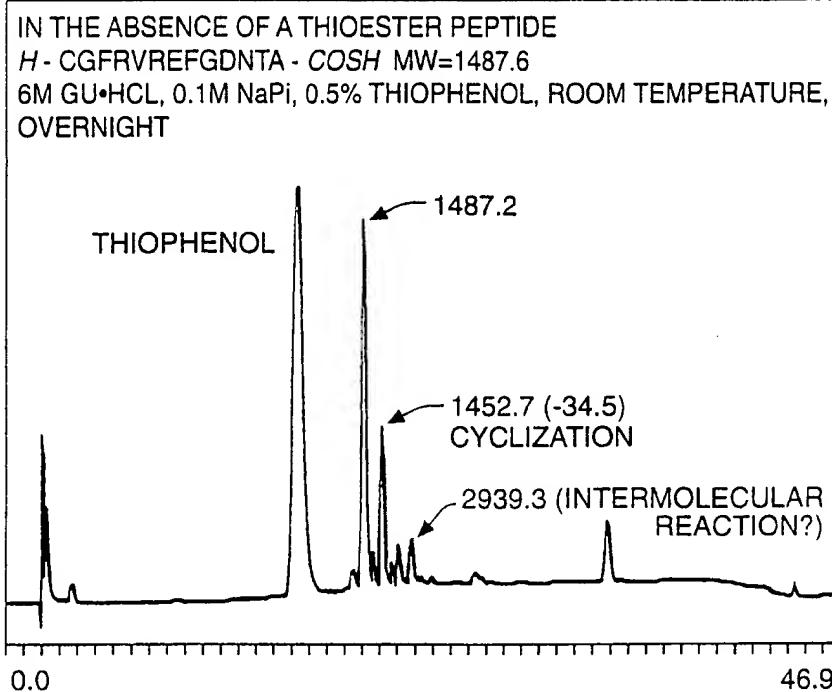
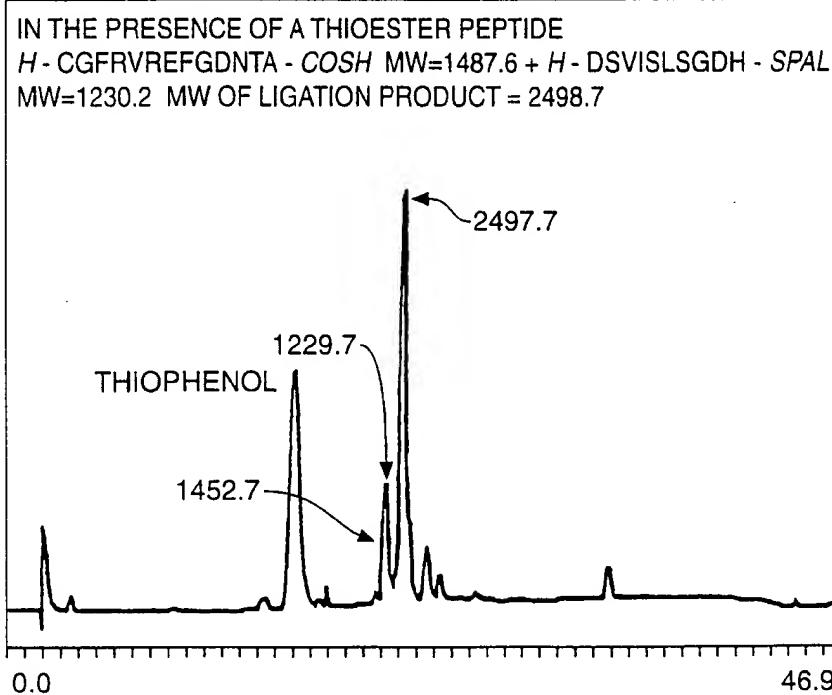
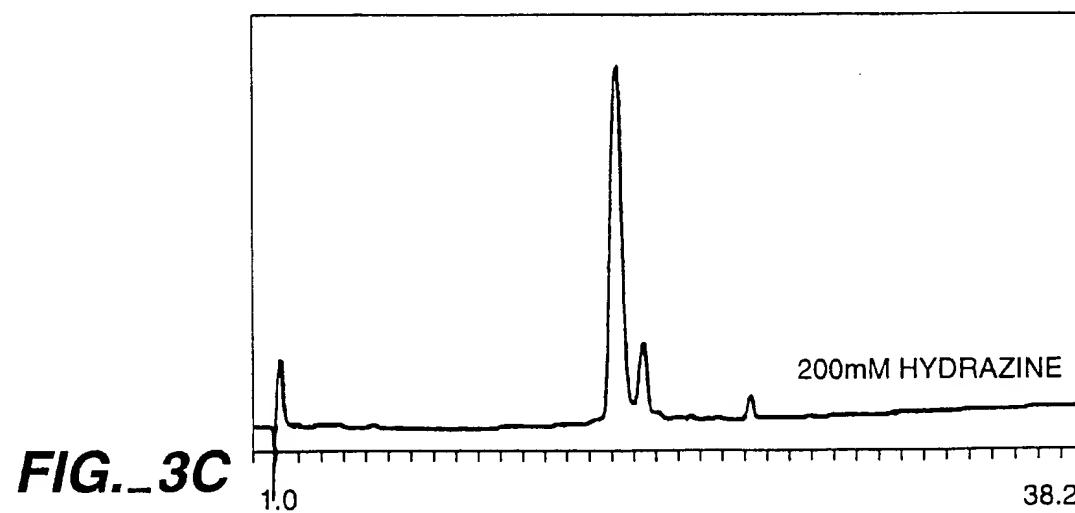
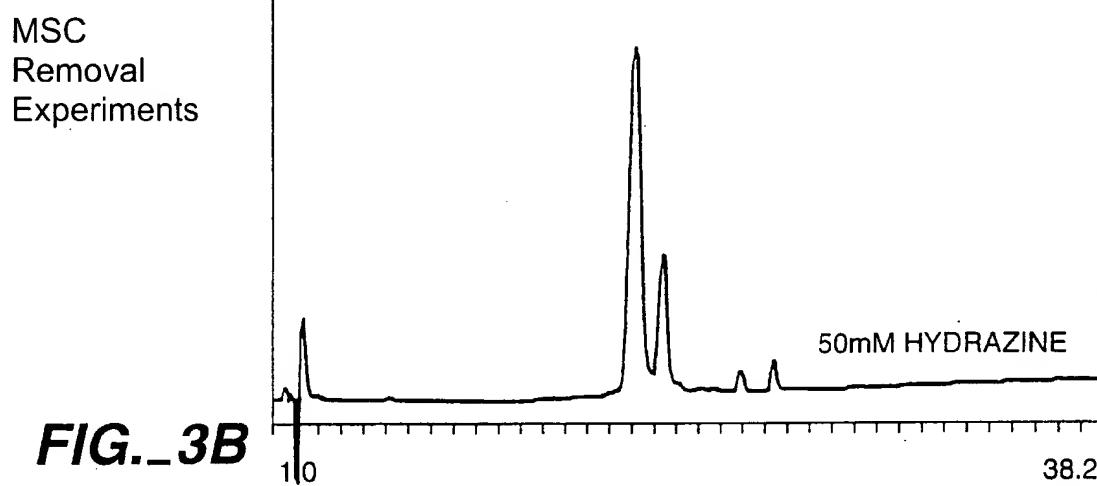
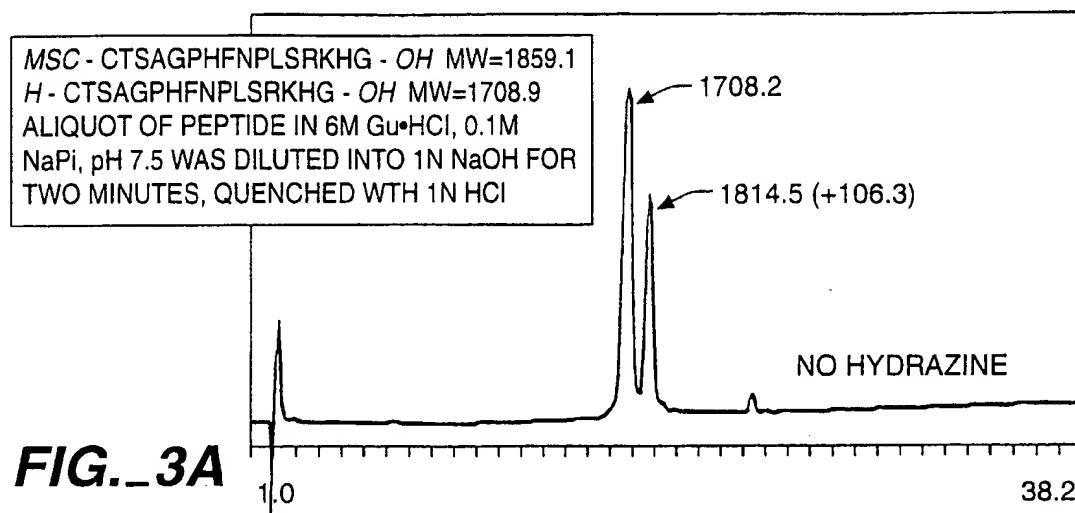


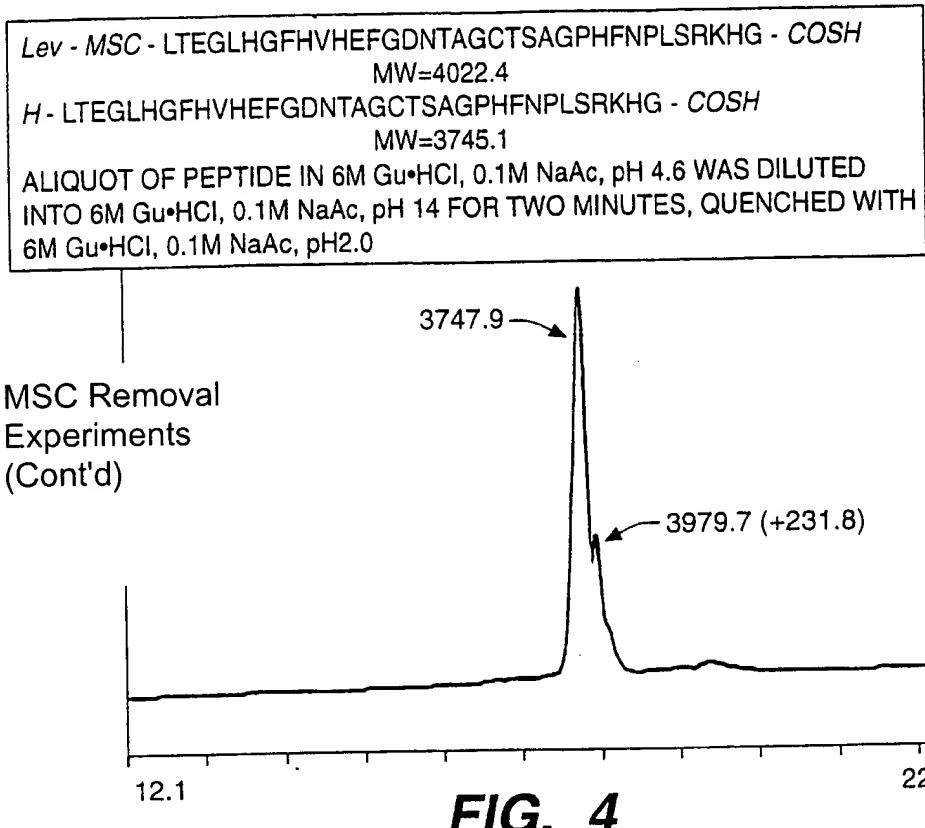
Scheme 1 Solid Phase Protein Synthesis  
 Native Chemical Ligations in an N- to C- Terminal Direction



**FIG.\_2A****FIG.\_2B**

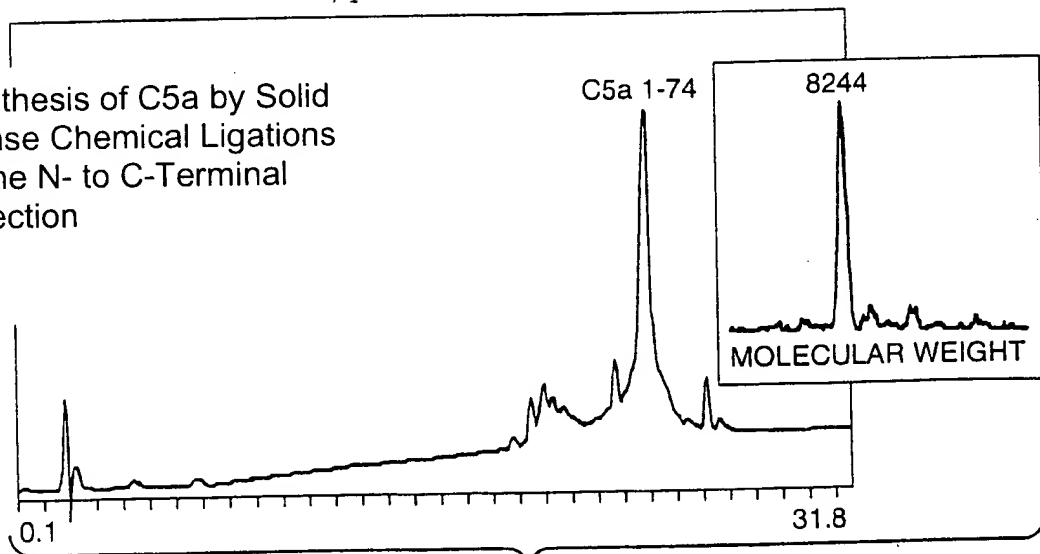
Cys +COSR Stability Under Ligation Conditions



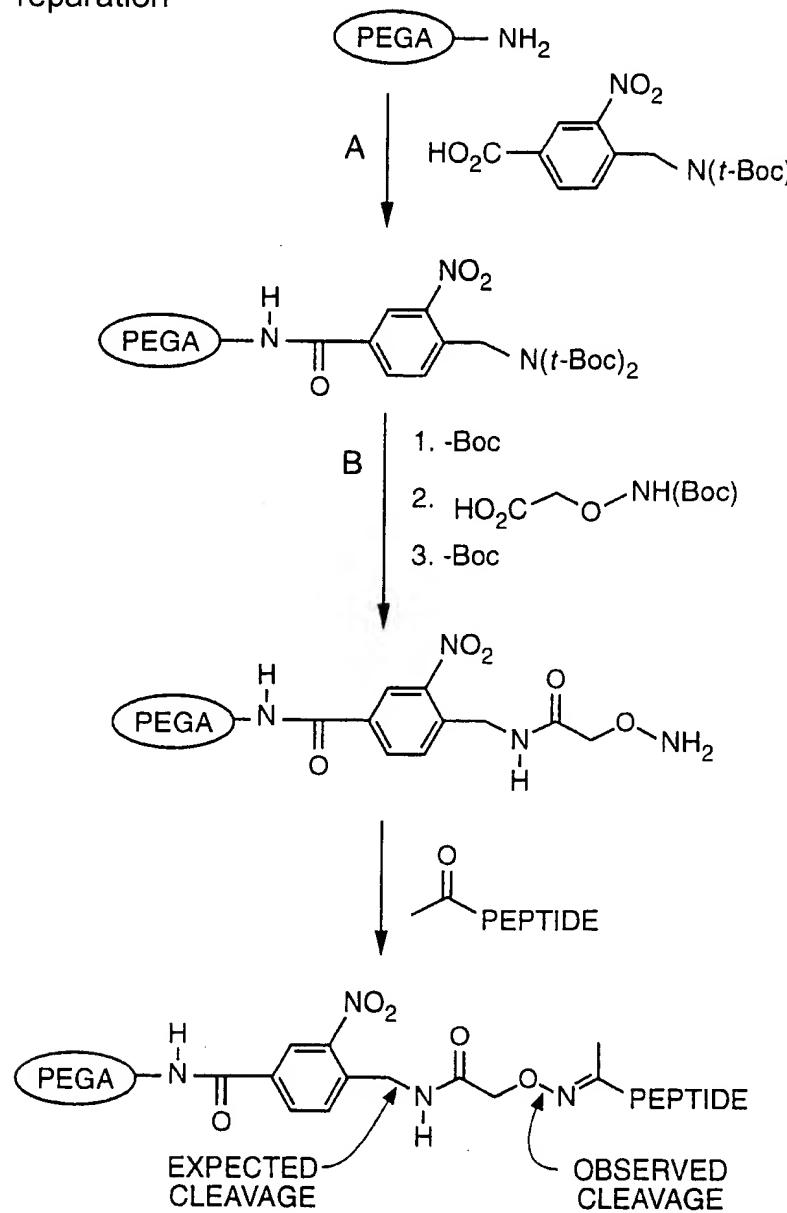
**FIG.\_4**

1 21 47  
 TLQKKIEEIAAKYKHSVVKCCYDGACVNNDTCEQRAARISLGPKCIKAFTECC  
 VVASQLRANISHKDMQLGR  
 74

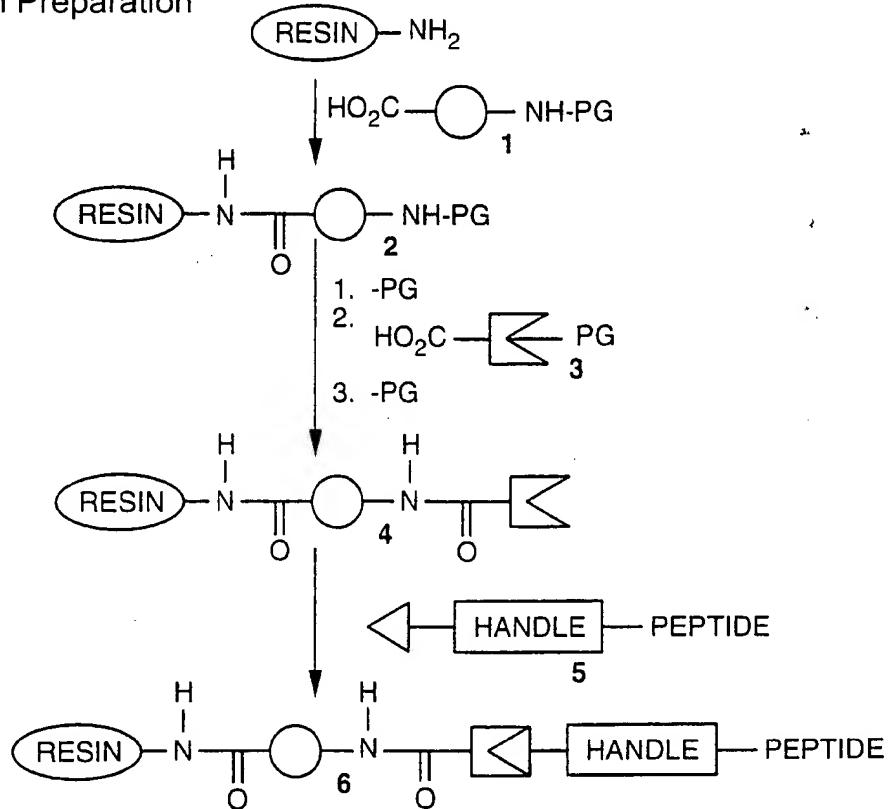
Synthesis of C5a by Solid Phase Chemical Ligations in the N- to C-Terminal Direction

**FIG.\_26**

## Resin Preparation

**FIG.\_5A**

## Resin Preparation



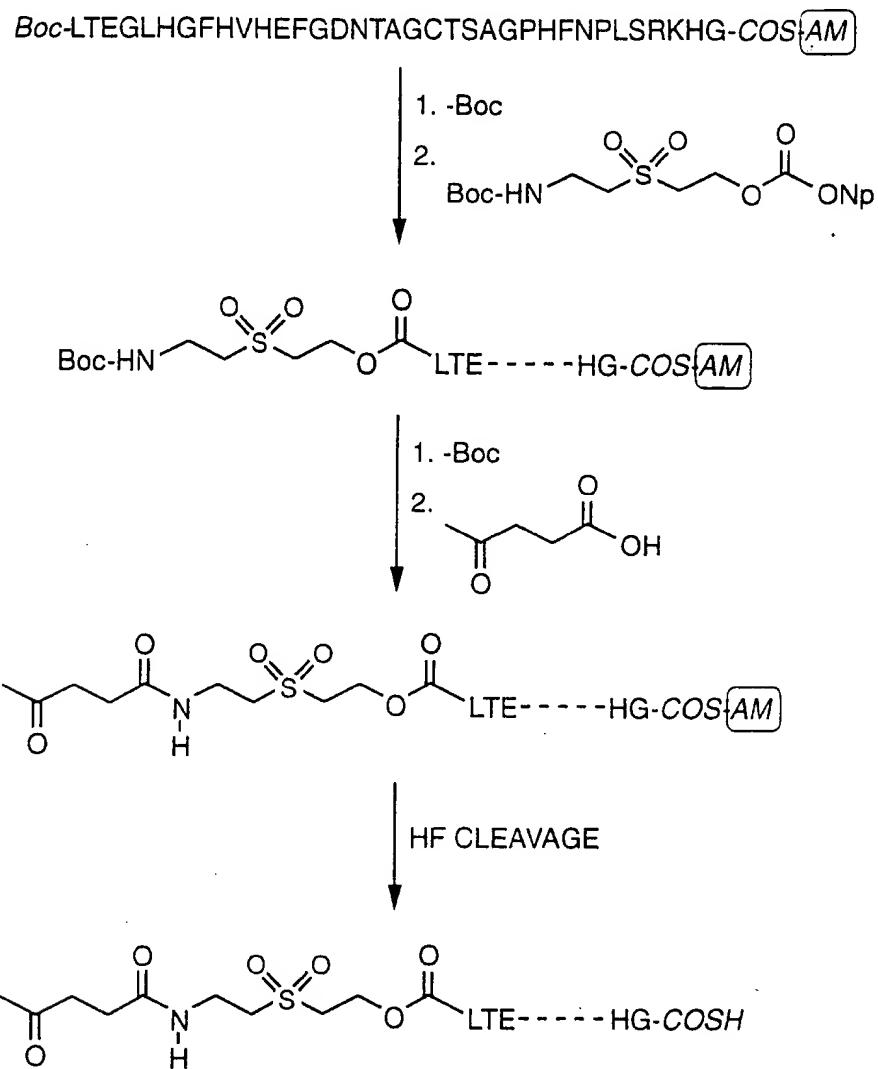
$\text{HO}_2\text{C}-\text{C}(=\text{O})-\text{NH-}$  = CLEAVABLE LINKER USED FOR MONITORING  
WITH MALDI, ELECTROSPRAY MASS  
SPECT, ETC...

PG = PROTECTING GROUP

$\text{HO}_2\text{C}-\text{C}(=\text{O})-$  = FUNCTIONAL GROUP ADDED TO RESIN TO  
COUPLE WITH PEPTIDE

$\text{HANDLE} \rightarrow \text{PEPTIDE}$  = PEPTIDE FUNCTIONALIZED WITH  
1. CLEAVABLE HANDLE FOR RELEASE OF  
PEPTIDE/PROTEIN FROM THE RESIN AT  
COMPLETION OF SYNTHESIS AND  
2. FUNCTIONAL GROUP TO COUPLE TO RESIN

**FIG. 5B**

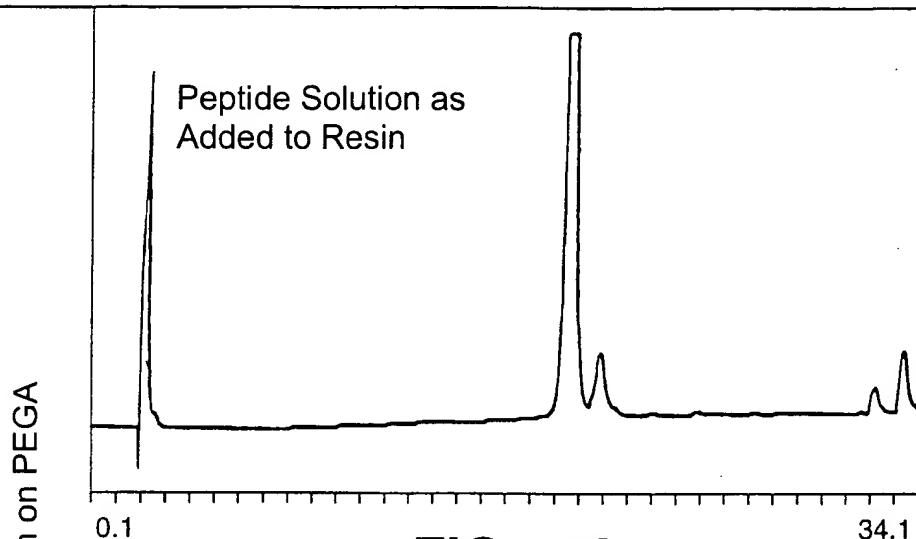
**FIG.\_6**

Derivatization of Segment 1  
(N-terminal)

*Lev - MSC - LTEGLHGFHVHEFGDNTAGCTSAGPHFNPLSRKHG - COSH (1)*  
+ Resin - PCL - ONH2

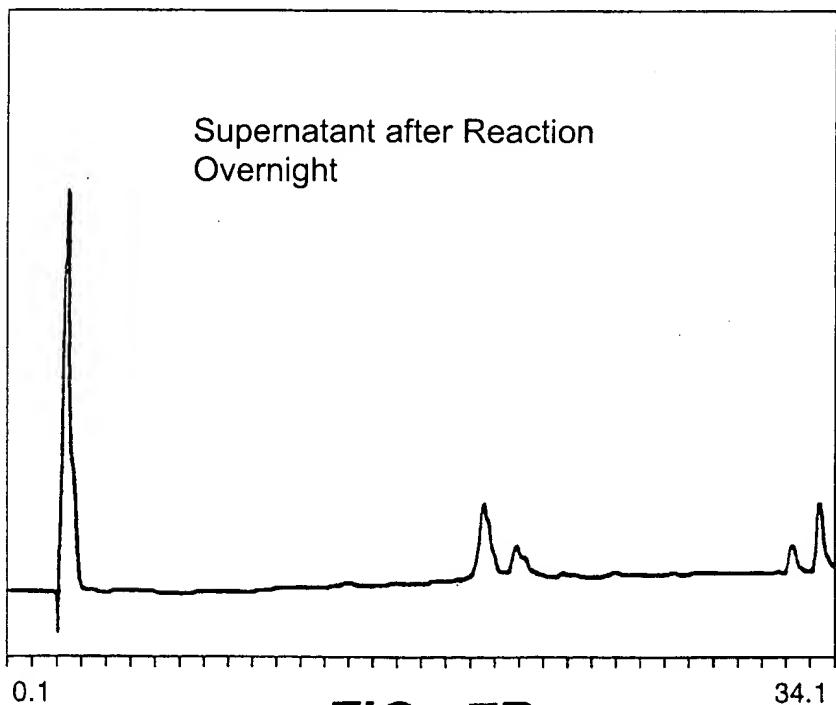
↓ 1. pH 4.6, 6M Gu-HCl, 0.1 ACETATE

Resin - PCL - oxime - MSC - LTEGLHGFHVHEFGDNTAGCTSAGPHFNPLSRKHG - COSH (1)



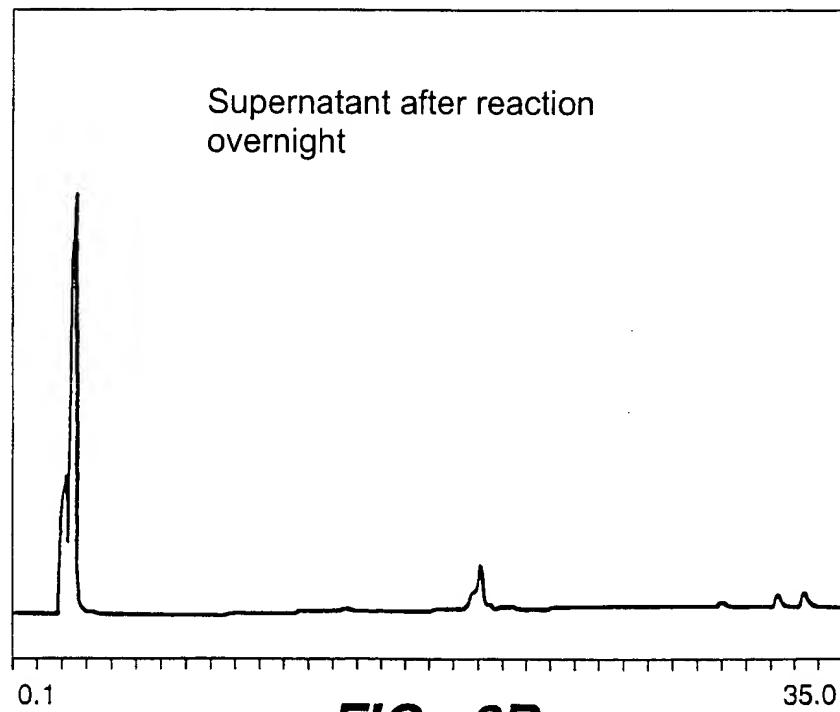
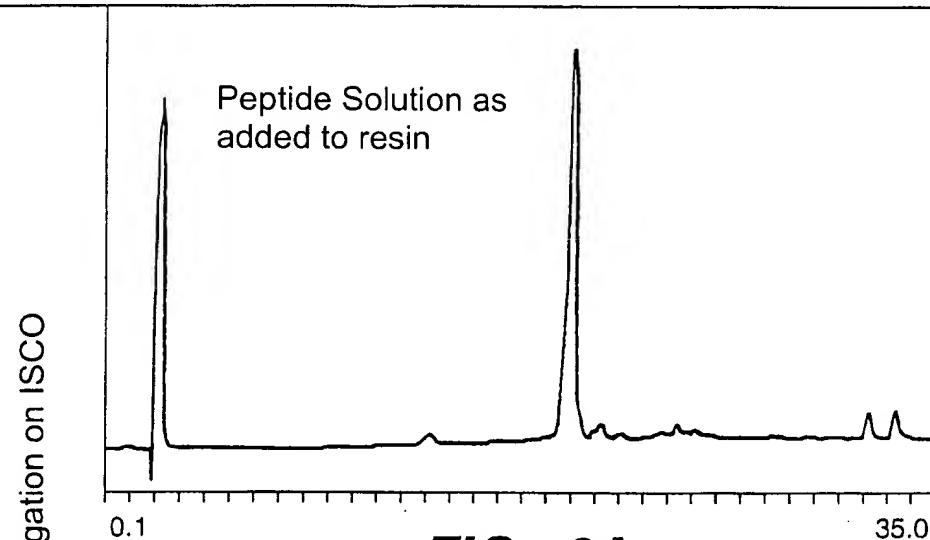
**FIG.-7A**

## Polymer-Supported Ligation on PEGA



**FIG.\_7B**

*Lev* - MSC - LTEGLHGFHVHEFGDNTAGCTSAGPHFNPLSRKHG - COSH (1)  
+ Resin - PCL - ONH<sub>2</sub>  
↓ 1. pH 4.6, 6M Gu•HCl, 0.1 ACETATE  
Resin - PCL - oxime - MSC - LTEGLHGFHVHEFGDNTAGCTSAGPHFNPLSRKHG - COSH (1)

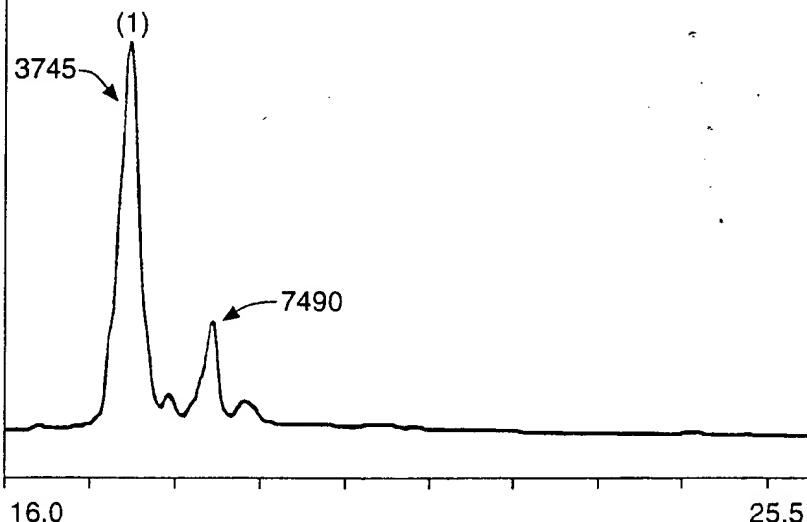


Lev - MSC - LTEGLHGFHVHEFGDNTAGCTSAGPHFNPLSRKHG - COSH (1)  
+ Resin - PCL - ONH2

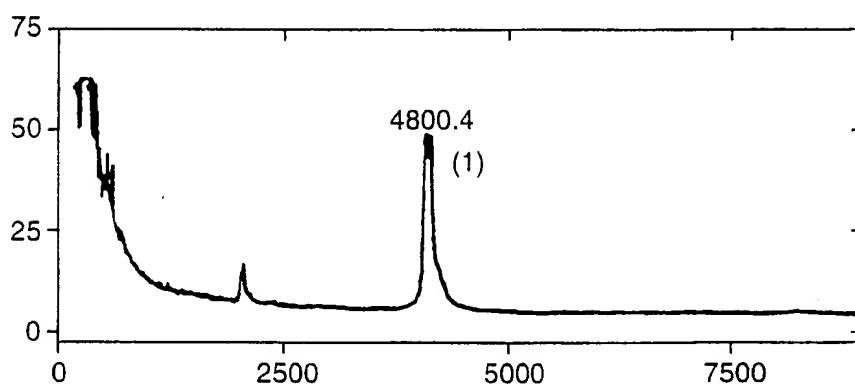
↓ 1. pH 4.6, 6M Gu-HCl, 0.1 ACETATE

Resin - PCL - oxime - MSC - LTEGLHGFHVHEFGDNTAGCTSAGPHFNPLSRKHG - COSH (1)  
MALDI MASS = 4022, BASE CLEAVAGE MASS = 3745

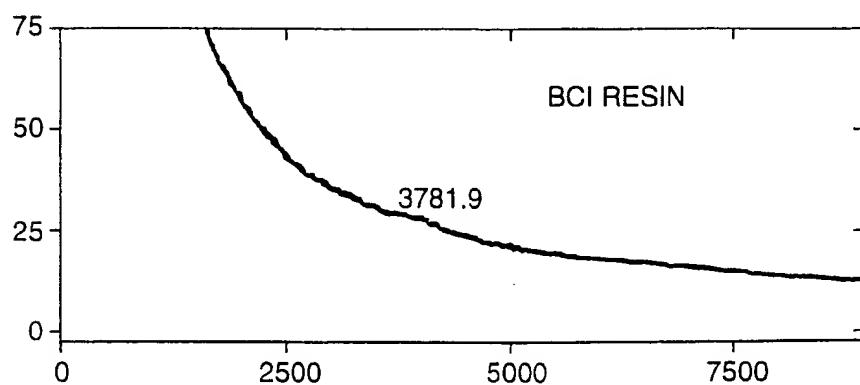
Polymer-  
Supported  
Ligation on  
ISCO



**FIG. 9A**



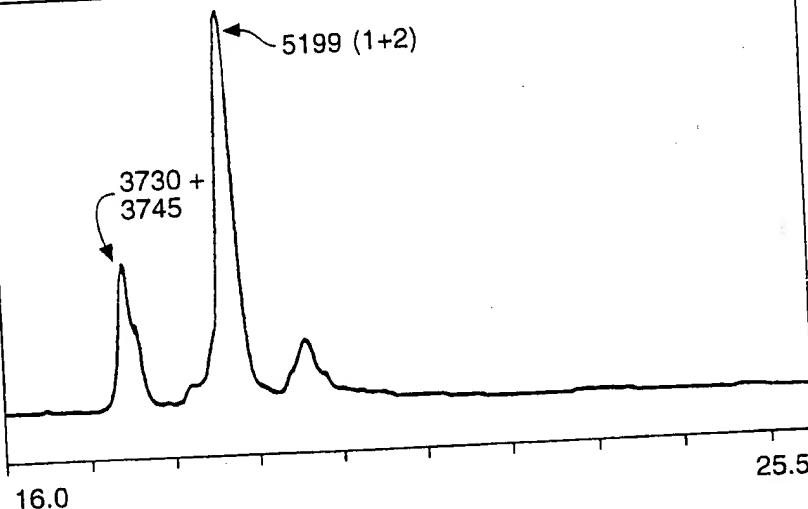
**FIG. 9B**



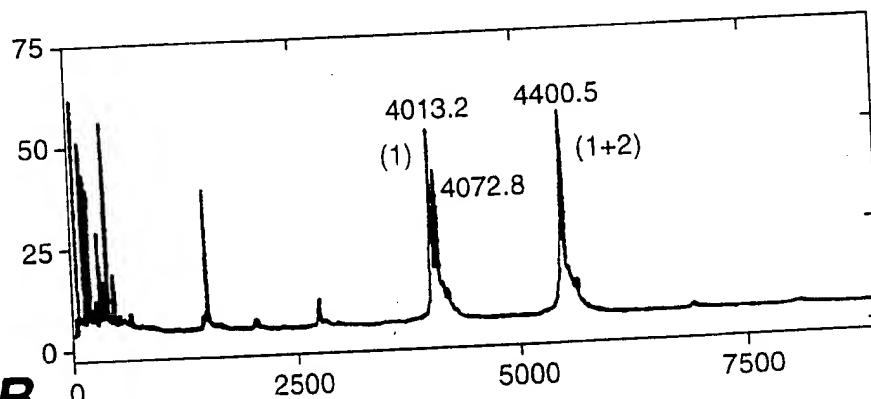
**FIG. 9C**

Resin - PCL - oxime - MSC - LTEGLHGTVHEFGDNTAGCTSAGPHFNPLSRKHG - COSAc (1)  
 MALDI MASS = 4080, BASE CLEAVAGE MASS = 3729  
 + H - CGFRVREFGDNTA - COSH (2)  
 ↓ 3. pH 7.5, 6M Gu-HCl, 0.1M PHOSPHATE, 0.5% THIOPHENOL  
 Resin - PCL - oxime - MSC - LTEGLHGTVHEFGDNTAGCTSAGPHFNPLSRKHGCGFRVREF -  
 GDNTA - COSH (1+2)  
 MALDI MASS = 5476, BASE CLEAVAGE MASS = 5199

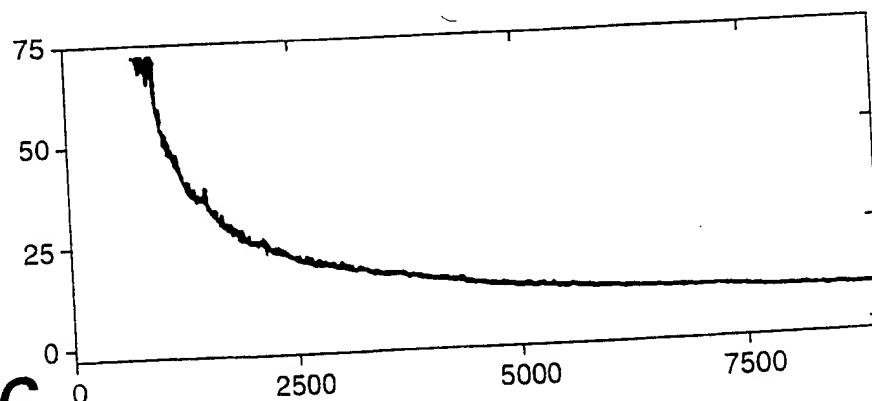
Polymer-  
Supported  
Ligation on  
ISCO



**FIG. - 10A**



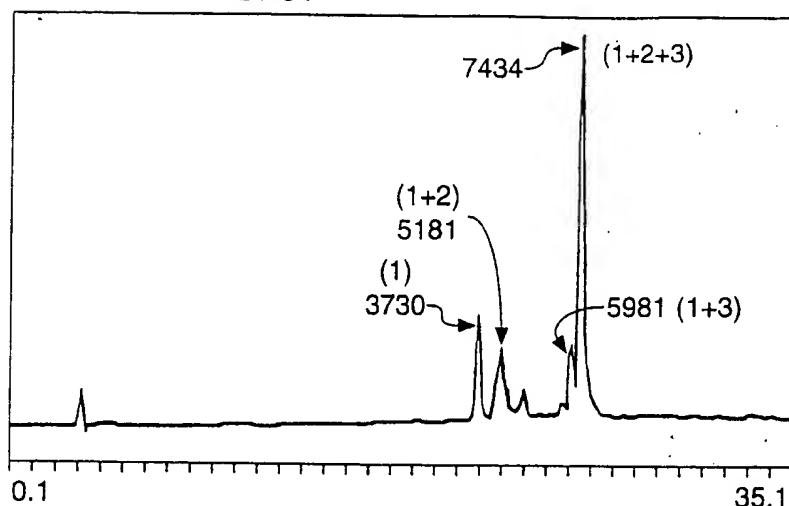
**FIG. - 10B**



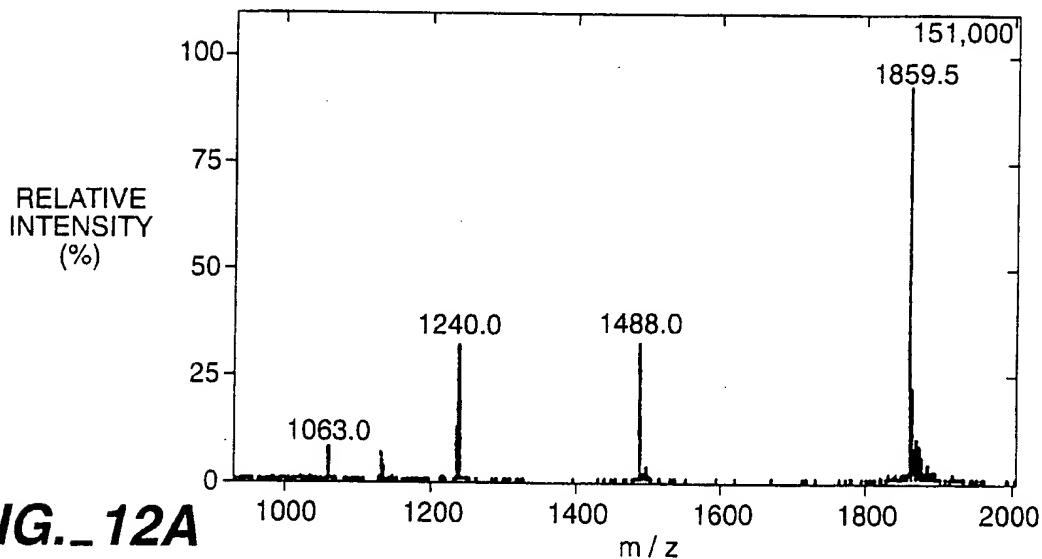
**FIG. - 10C**

Polymer-  
Supported  
Ligation on ISCO

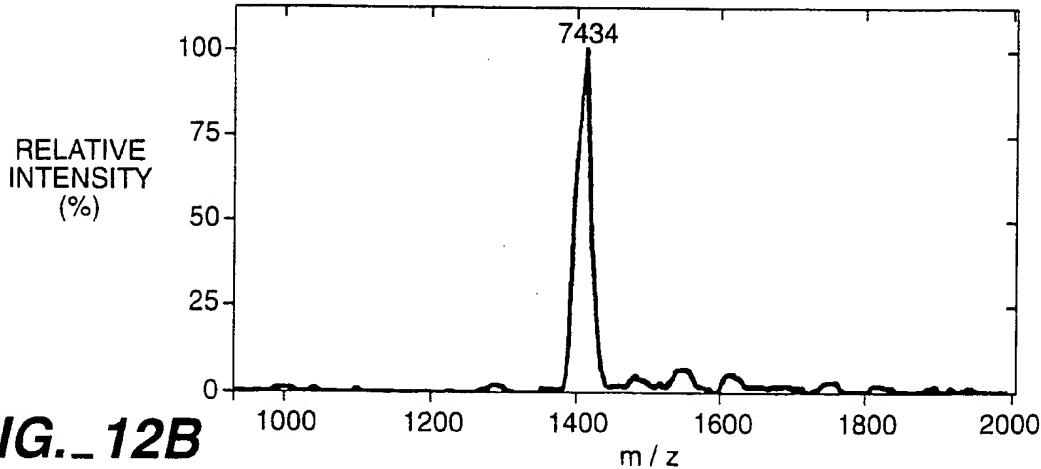
**FIG.\_ 11**



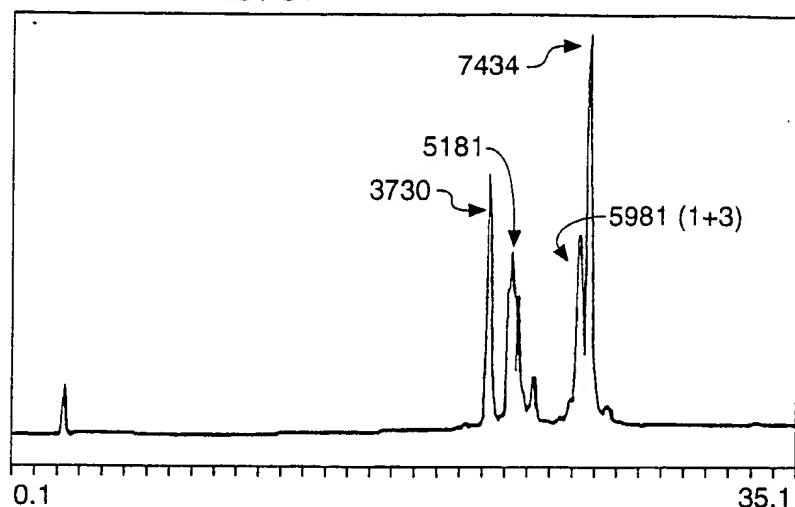
**FIG.\_ 12A**



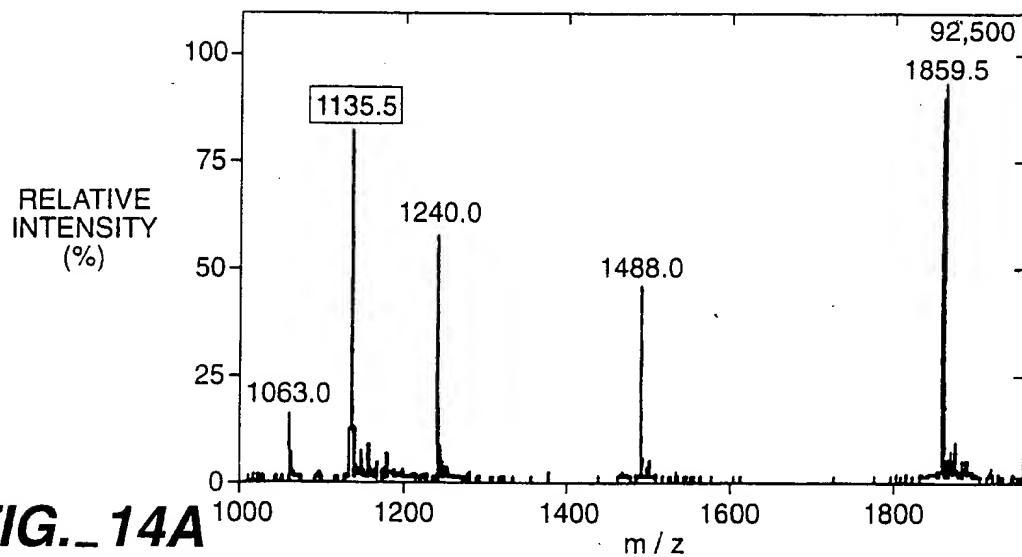
**FIG.\_ 12B**



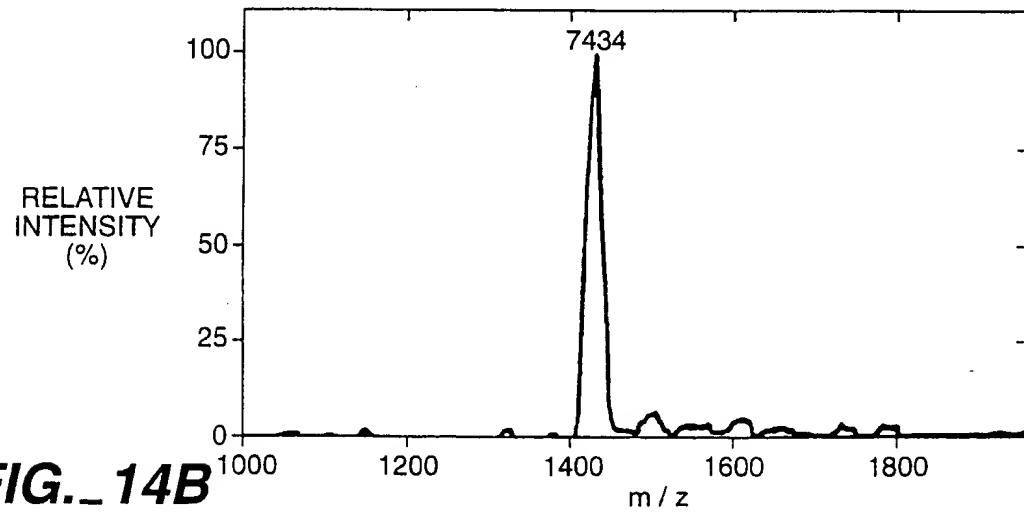
Polymer-Supported Ligation on PEGA



**FIG.\_ 13**

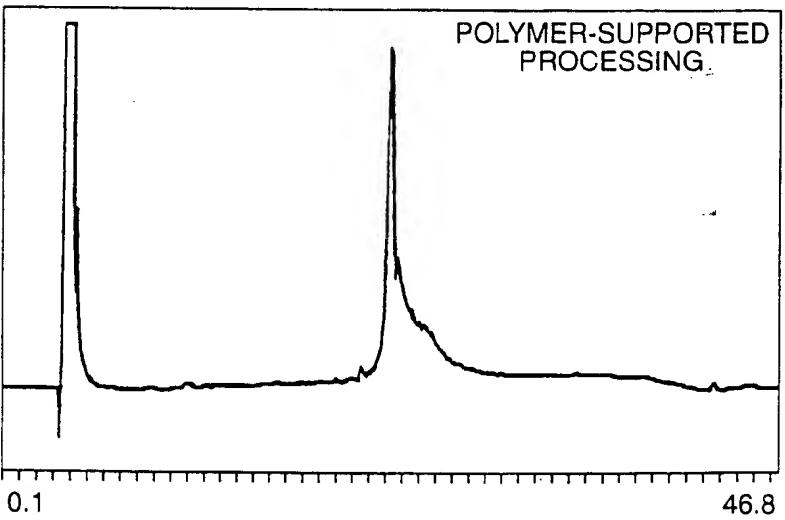
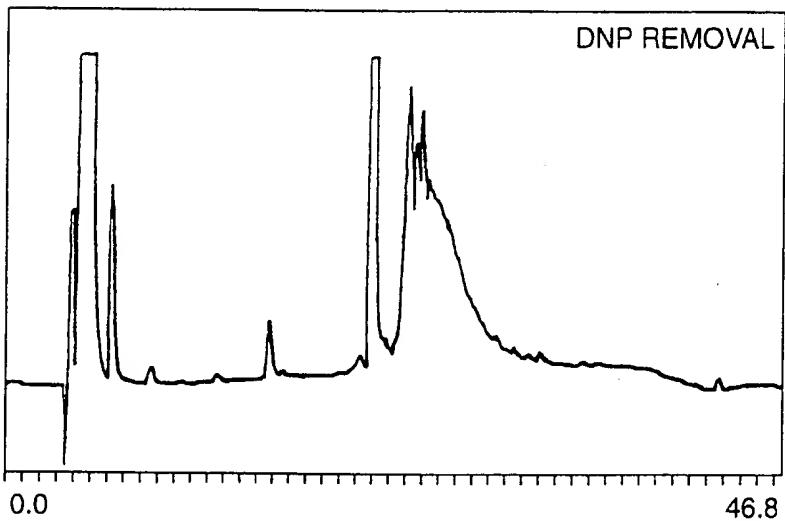
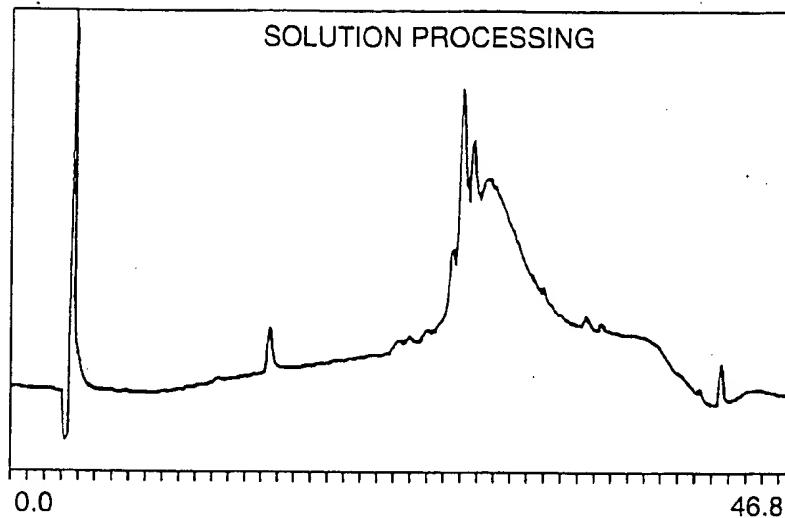


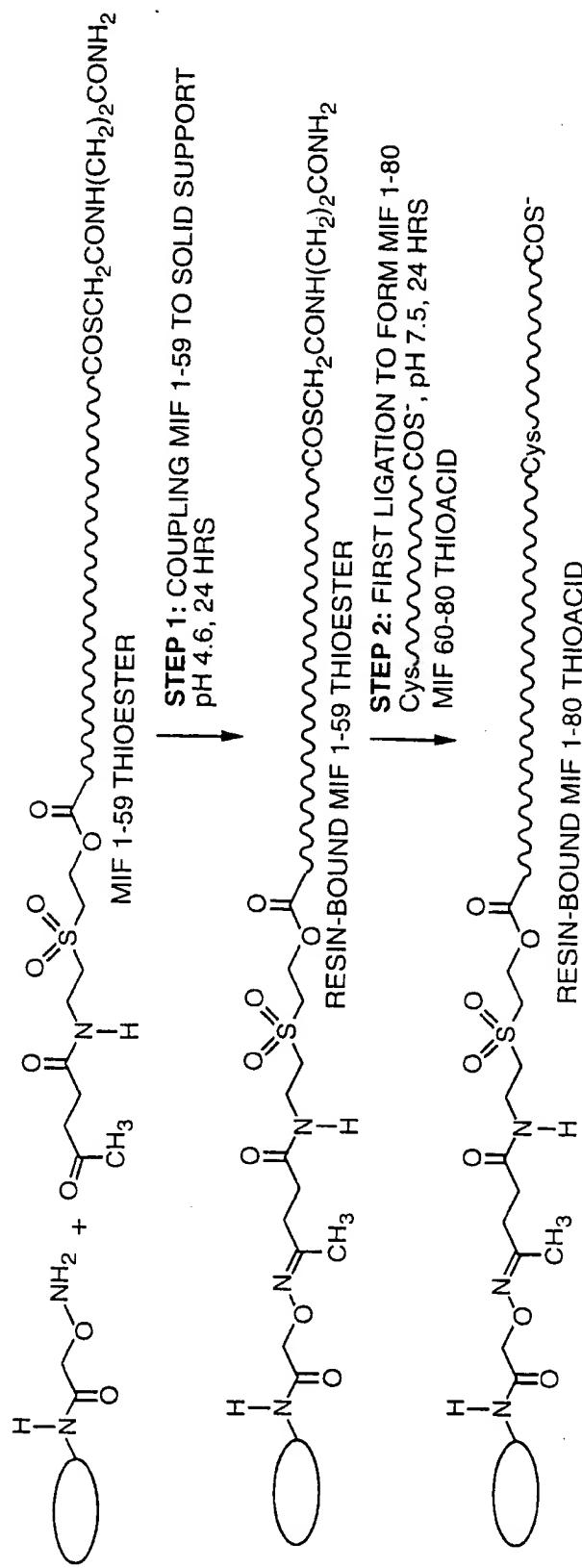
**FIG.\_ 14A**



**FIG.\_ 14B**

On Resin  
Purification



**FIG. 16A**

Synthesis of MIIF by Solid Phase Native Ligations

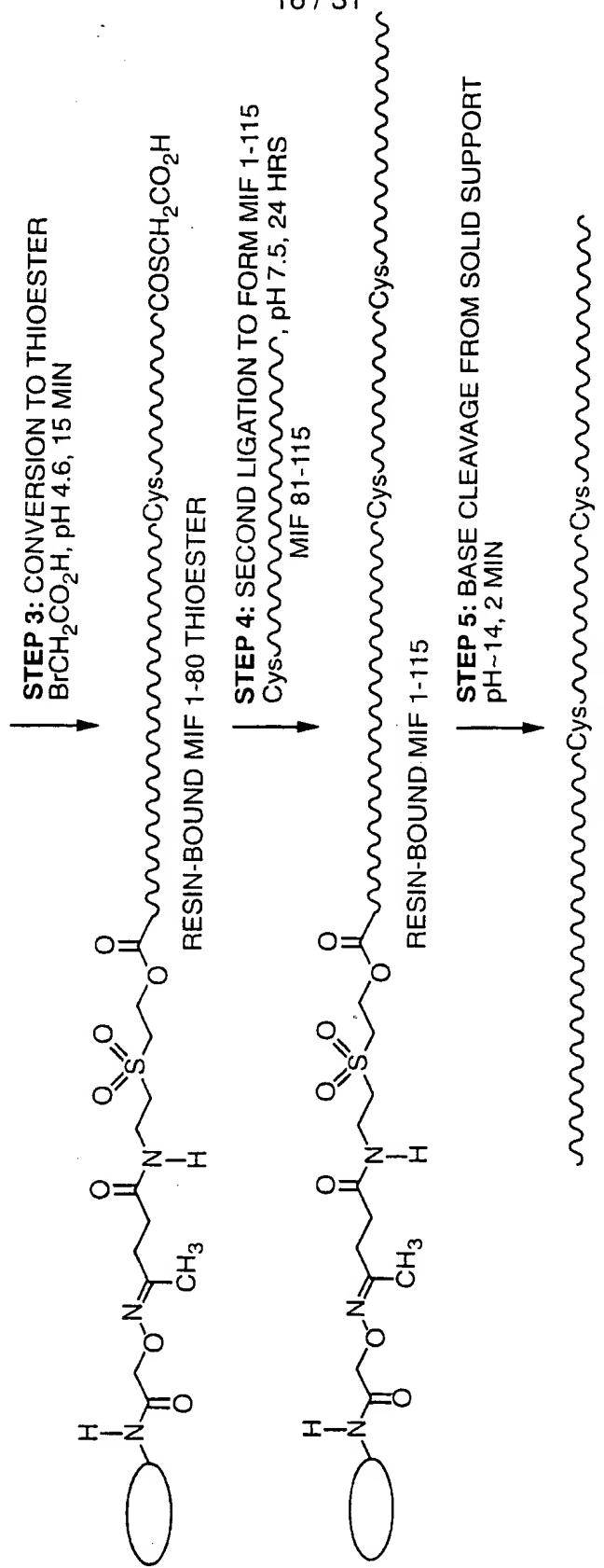
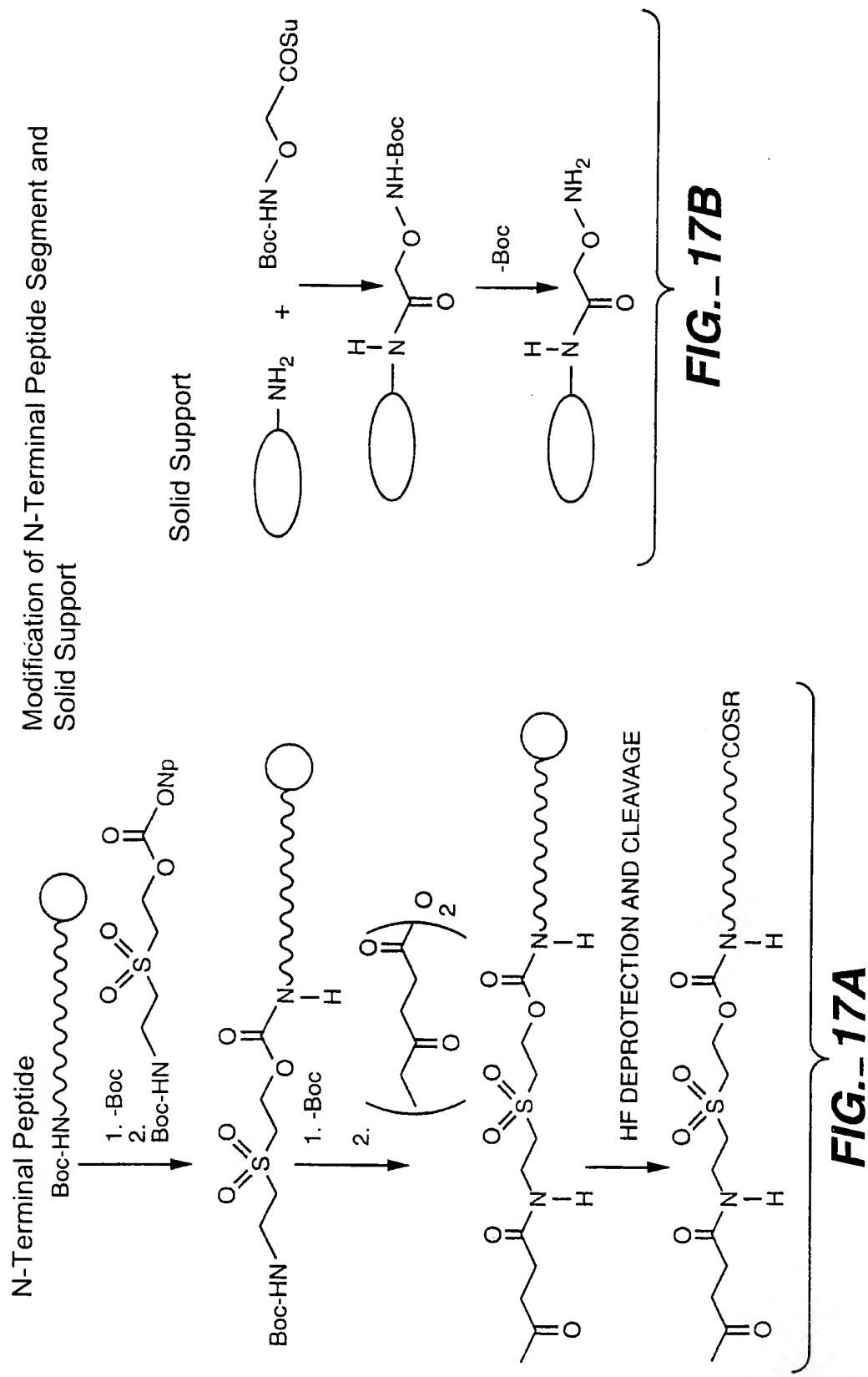
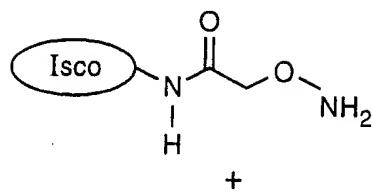


FIG. - 16B

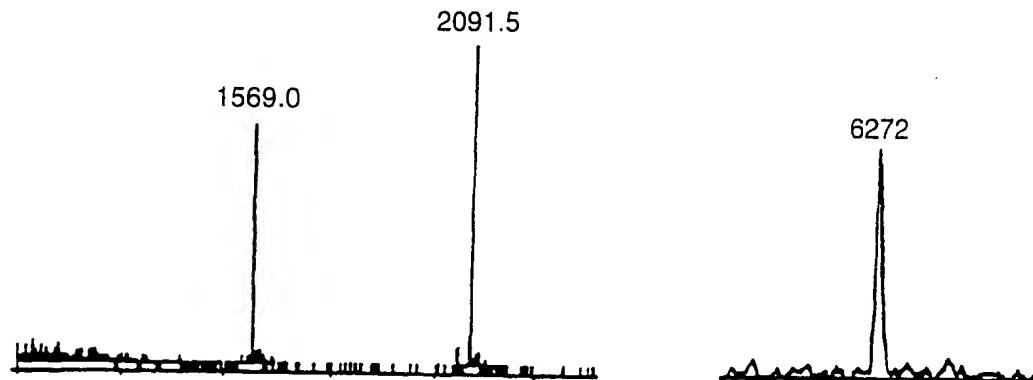


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Coupling of MIF  
1-59 to Solid  
Support

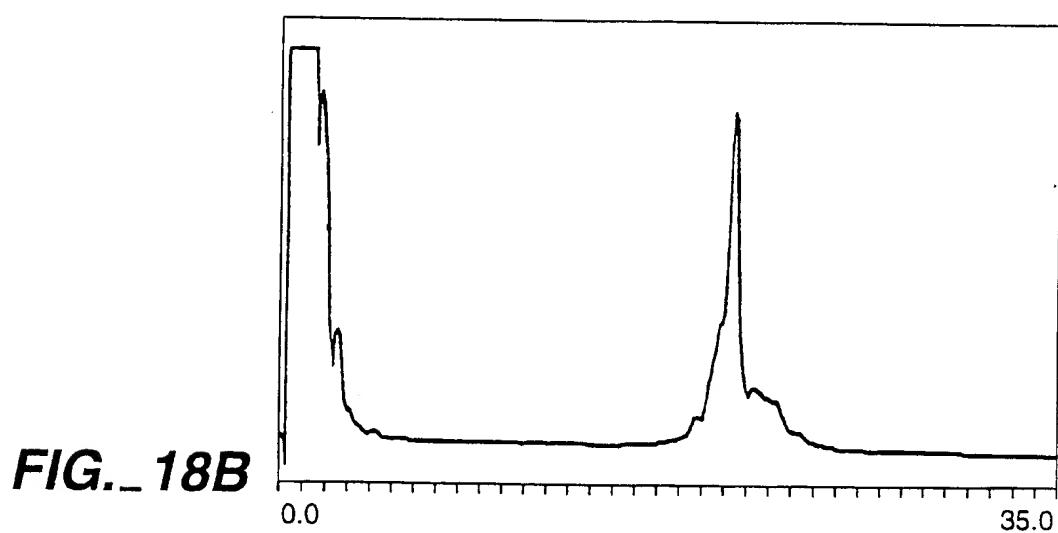


**FIG. 18A**



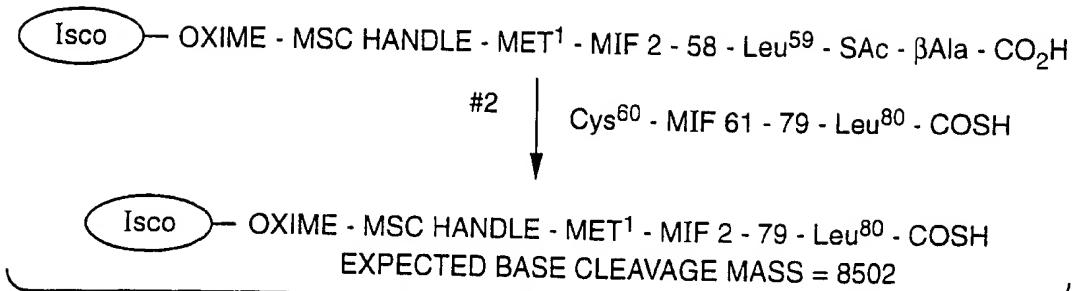
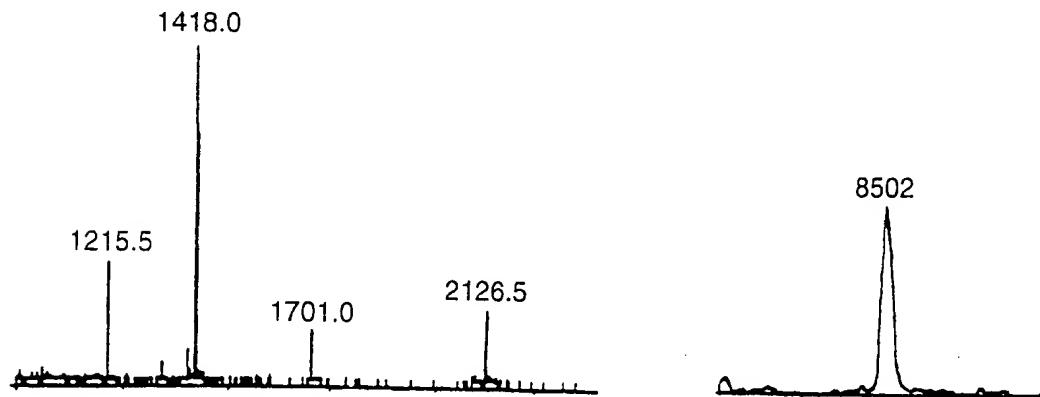
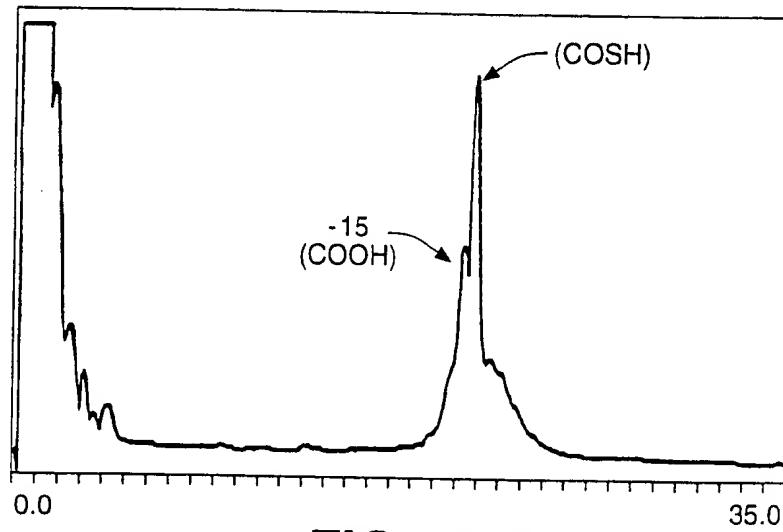
**FIG. 18C**

**FIG. 18D**



**FIG. 18B**

## Ligation to form MIF 1-80

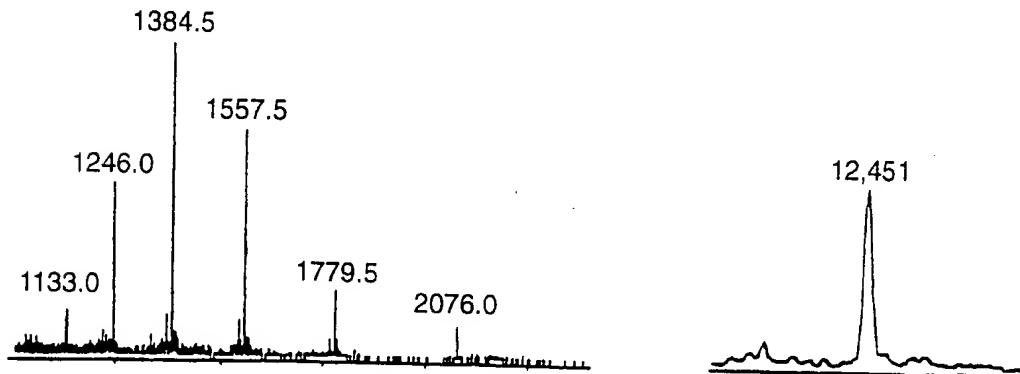
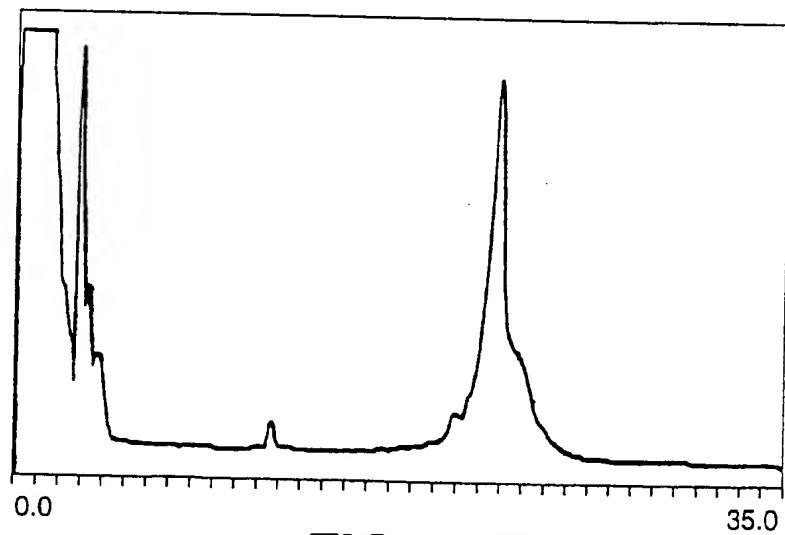
**FIG.\_ 19A****FIG.\_ 19C****FIG.\_ 19D****FIG.\_ 19B**

## Ligation to form MIF 1-115

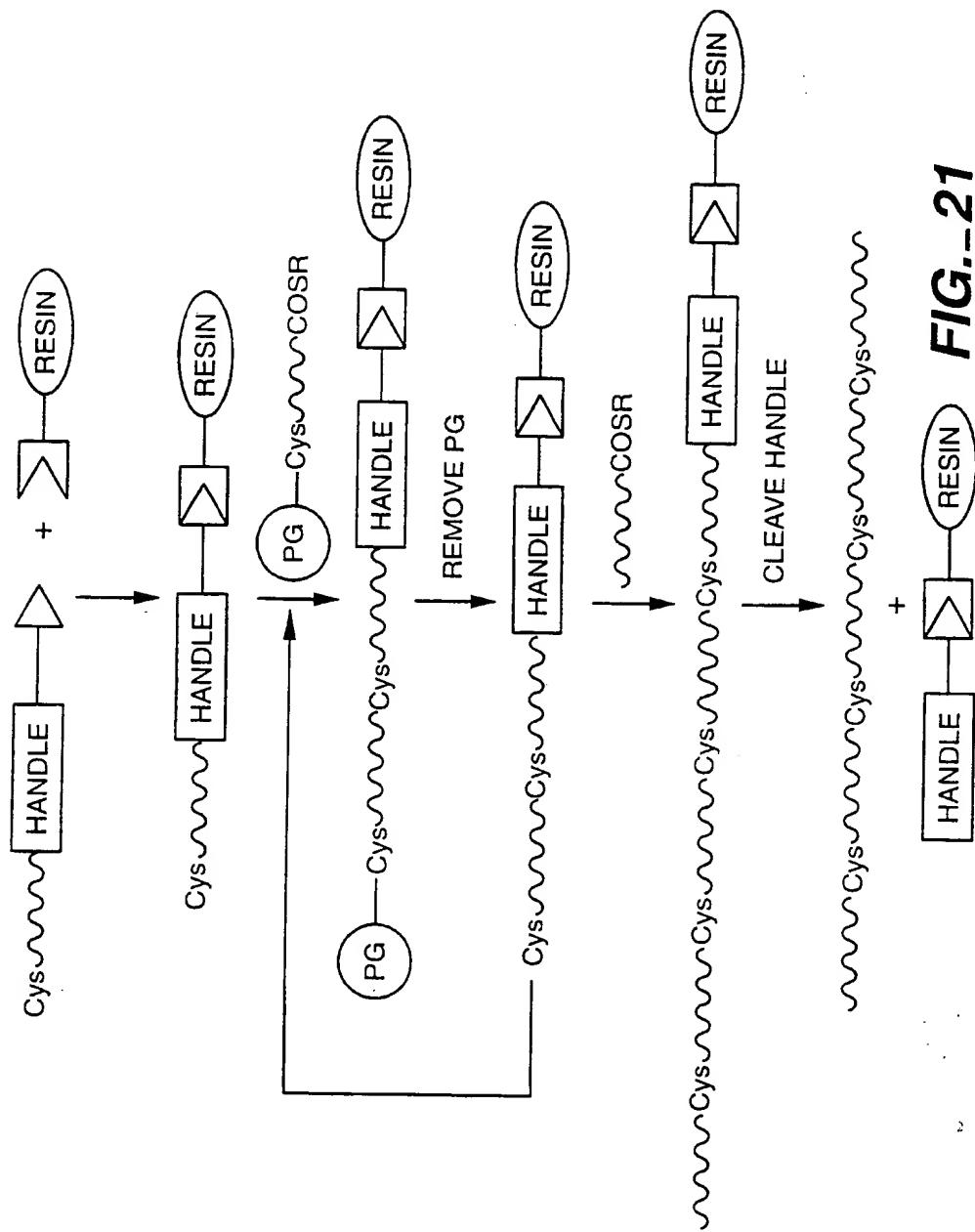
Isco — OXIME - MSC HANDLE - MET<sup>1</sup> - MIF 2 - 79 - Leu<sup>80</sup> - COSAc

#4      Cys<sup>81</sup> - MIF 82 - 114 - Ala<sup>115</sup> - CO<sub>2</sub>H  
 6M Gu•HCl, 0.1, 0.1 M Na Pi, 0.5% THIOPHENOL  
 0.15 M METHIONINE, pH 7.5

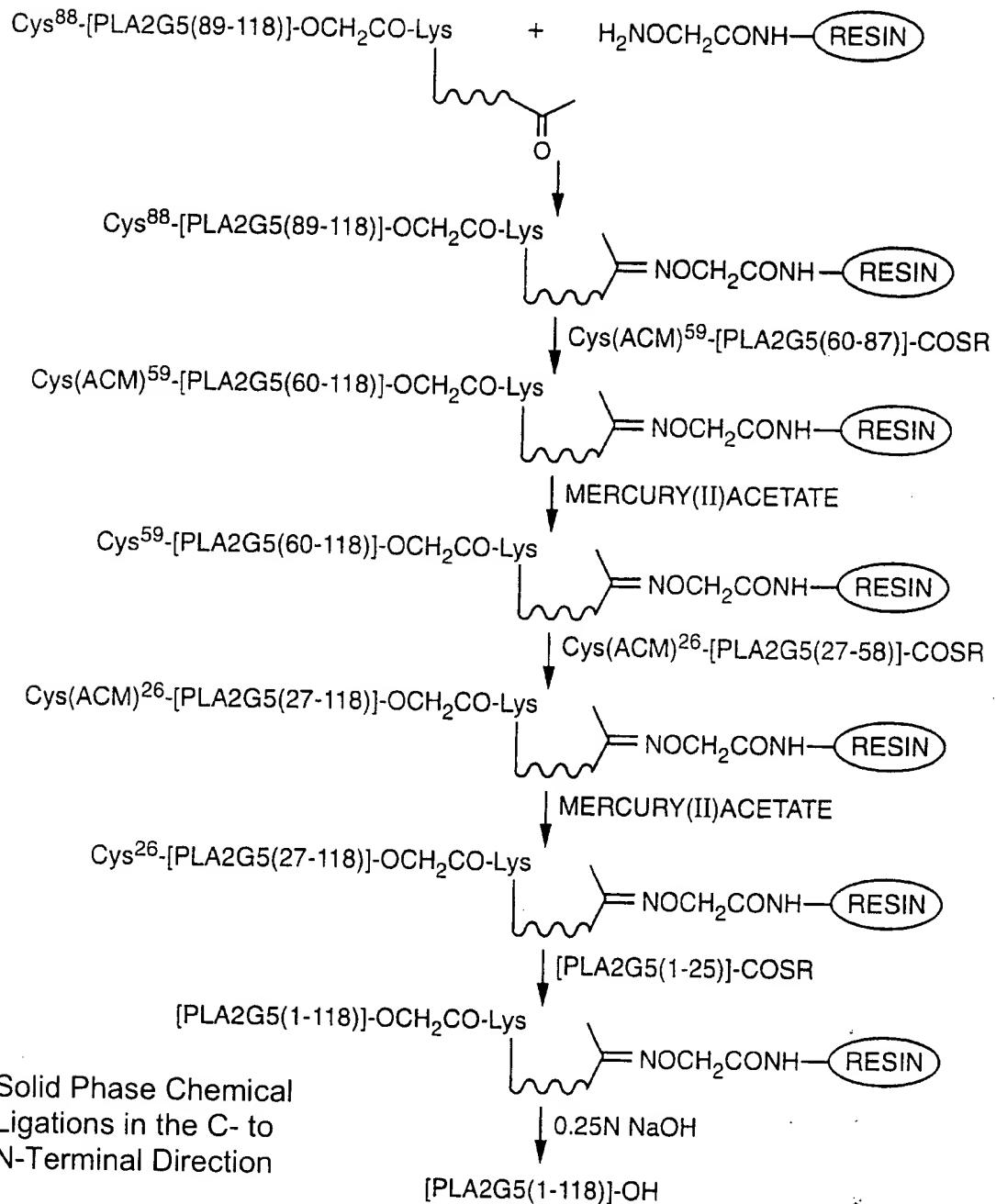
Isco — OXIME - MSC HANDLE - MET<sup>1</sup> - MIF 2 - 114 - Ala<sup>115</sup> - CO<sub>2</sub>H  
 EXPECTED BASE CLEAVAGE MASS = 12450

**FIG.\_20A****FIG.\_20C****FIG.\_20D****FIG.\_20B**

Solid Phase Chemical Ligations in the  
C- to N-terminal Direction

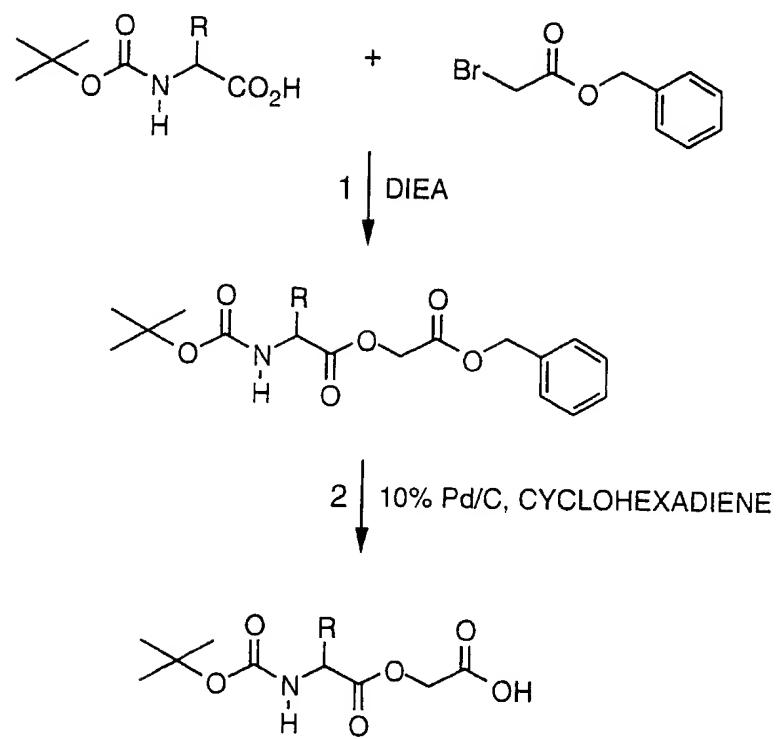


**FIG.-21**



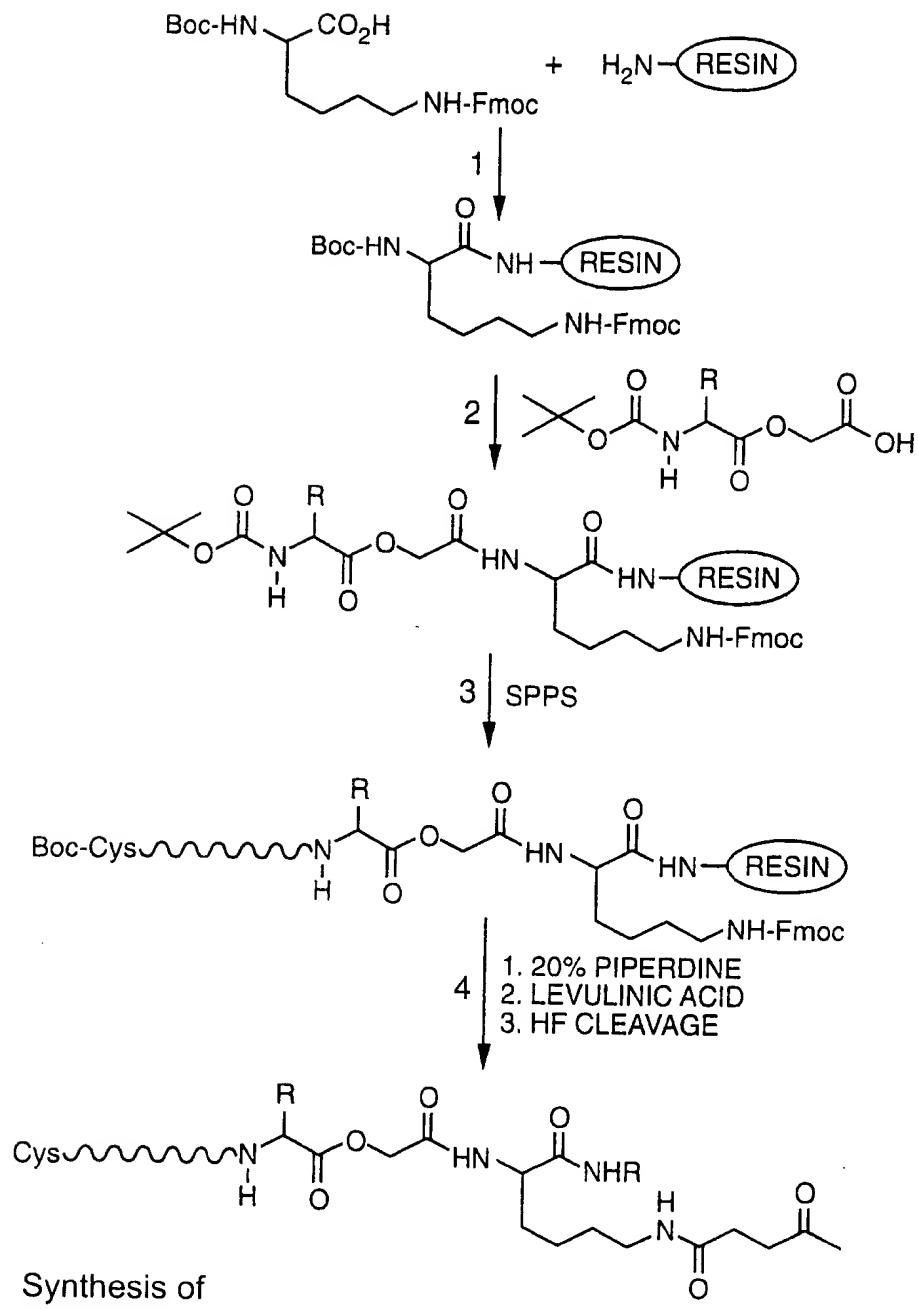
## Synthesis of Phospholipase A2, Group 5 (PLA2G5)

**FIG. 22**



**FIG.. 23**

Synthesis of Cam ester derivative

**FIG.\_24**

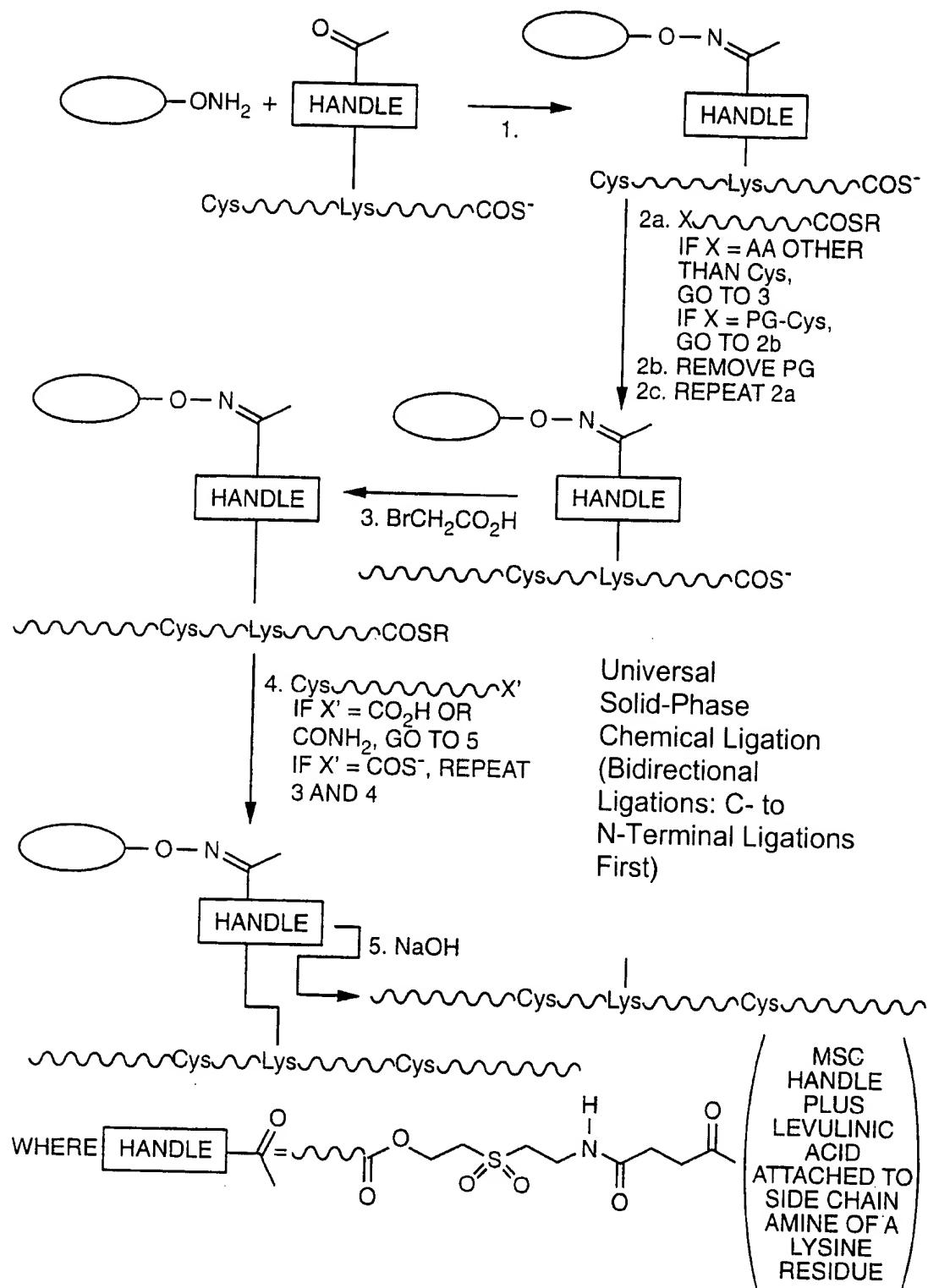


FIG.-25A

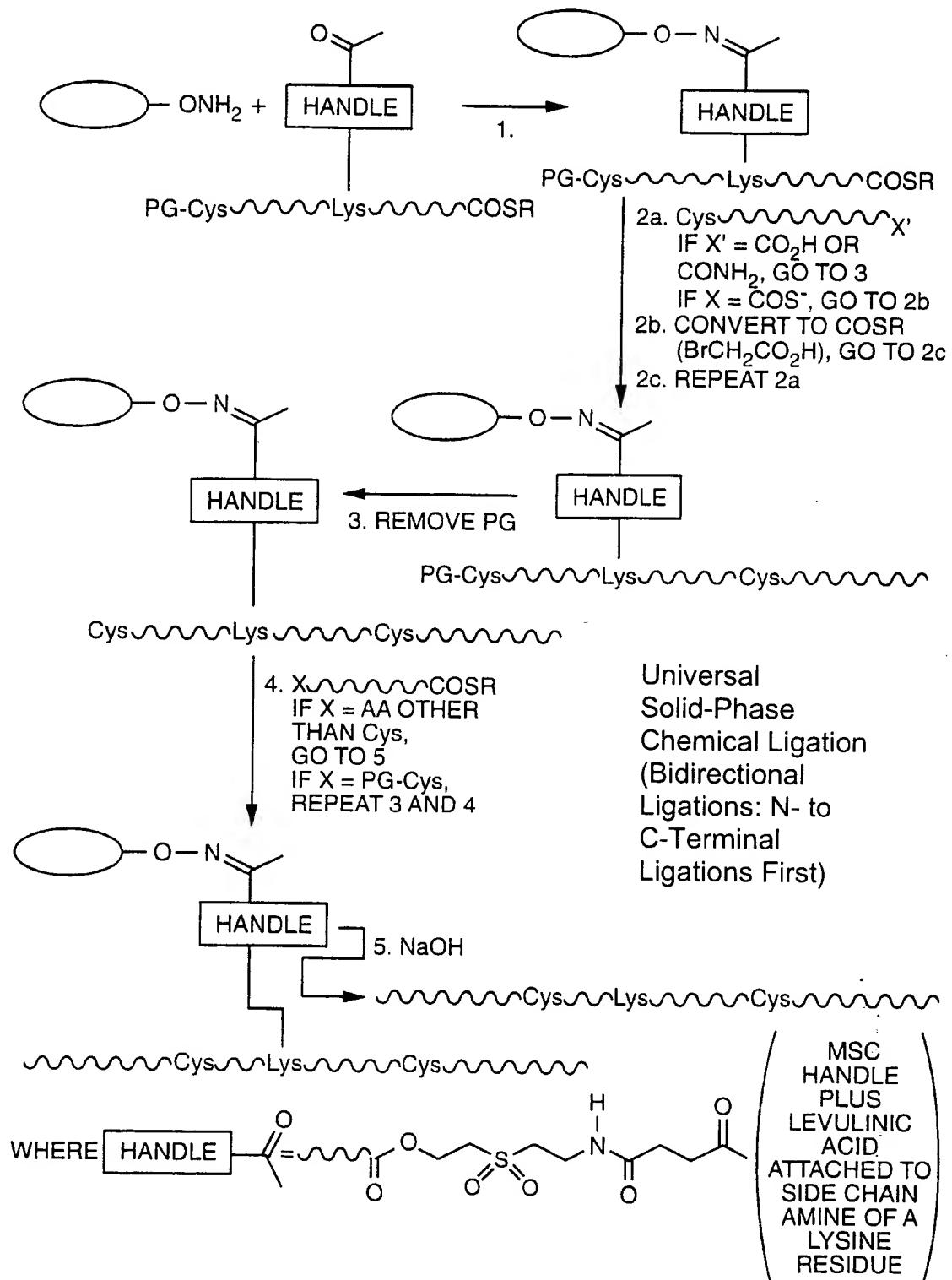
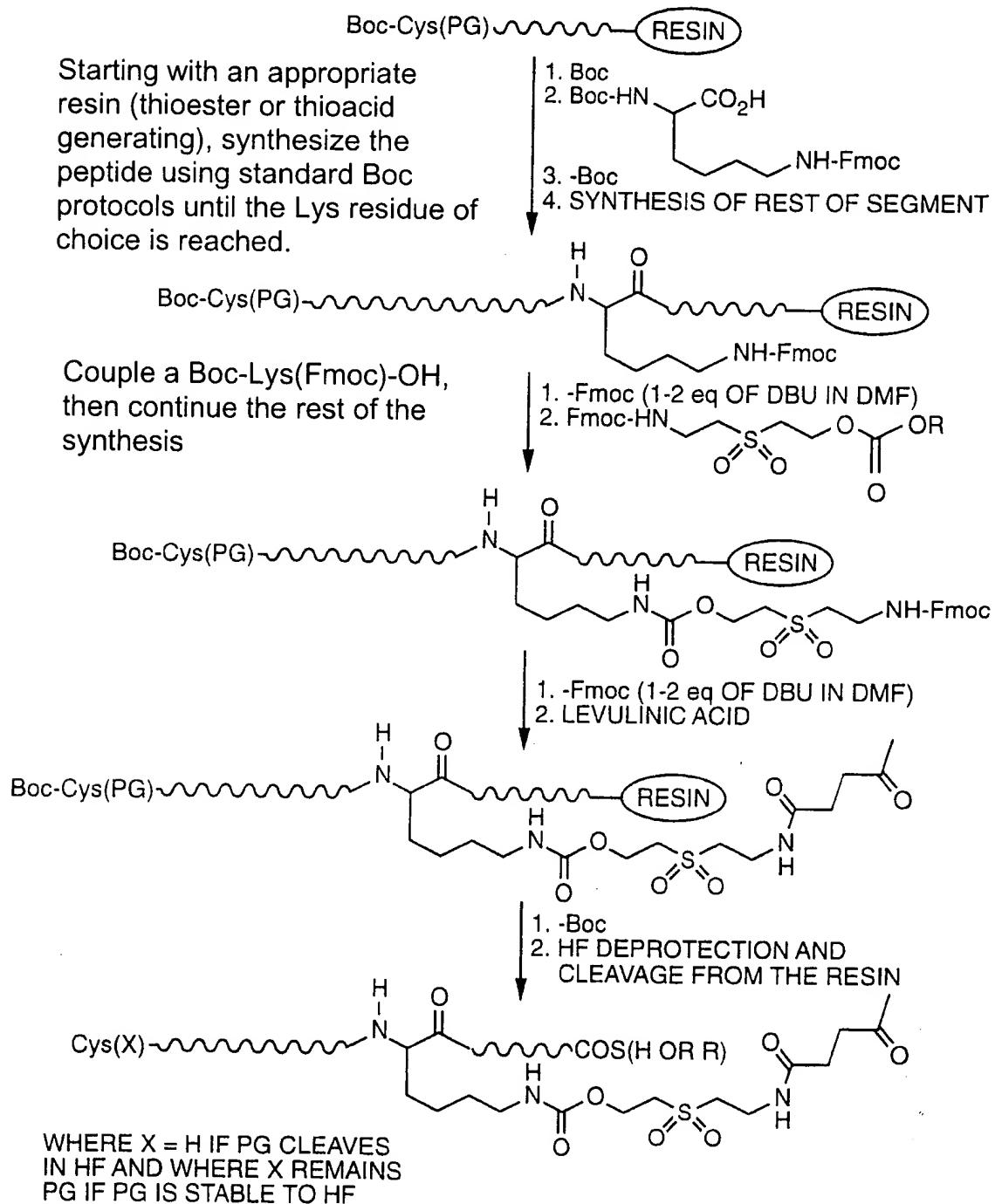
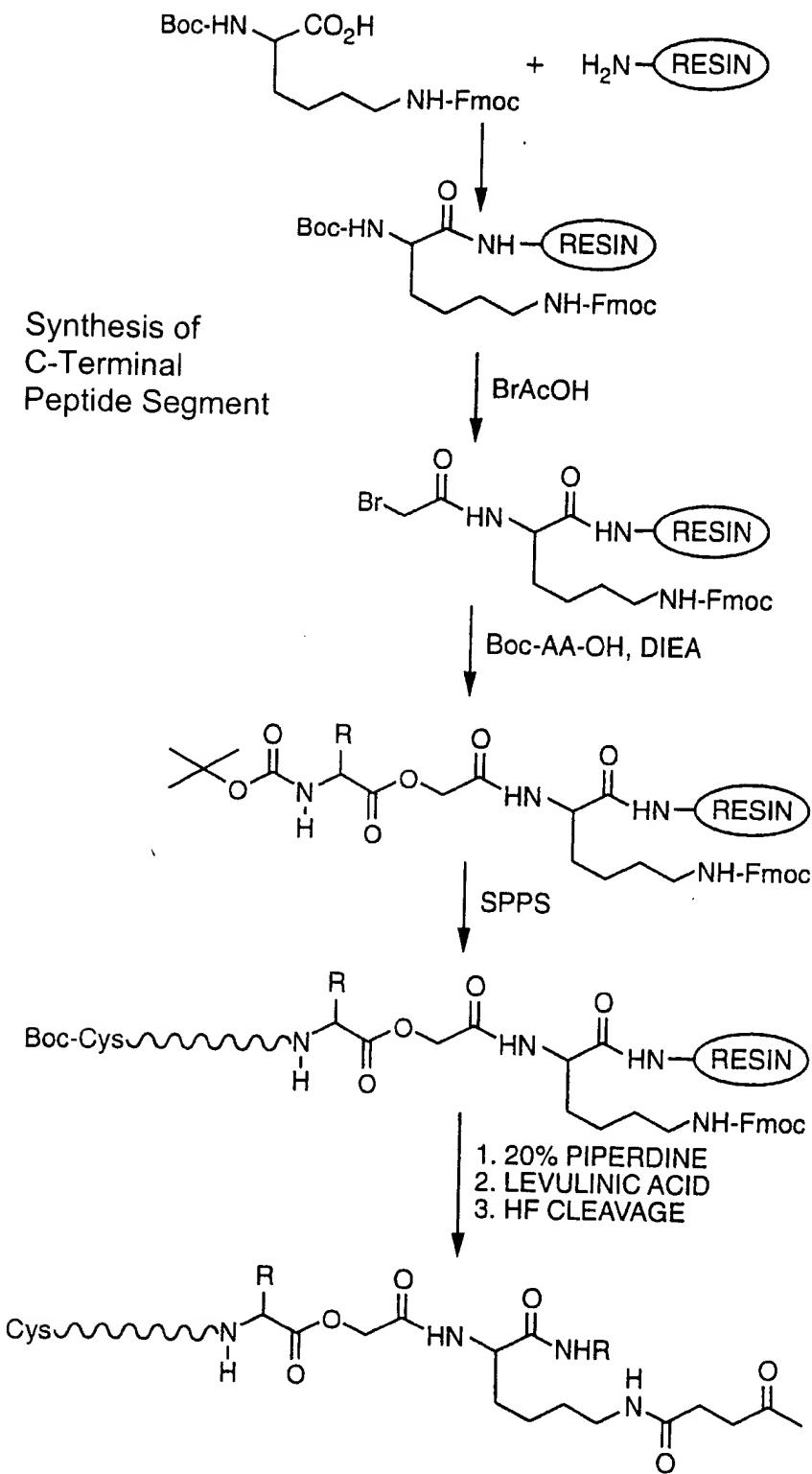


FIG.-25B

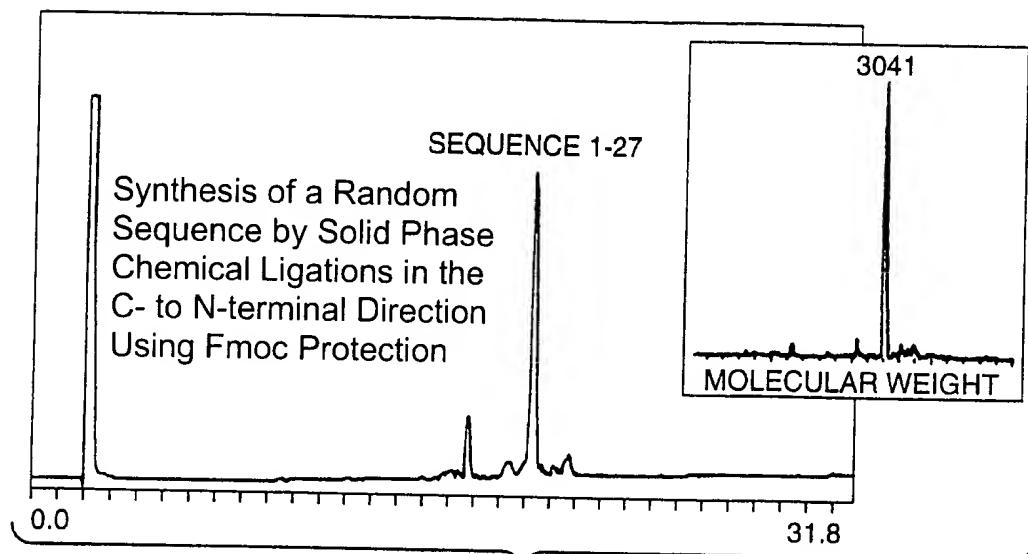
**Synthesis of Modified Peptide Segment for Universal Solid Phase Chemical Ligation**



**FIG.-25C**

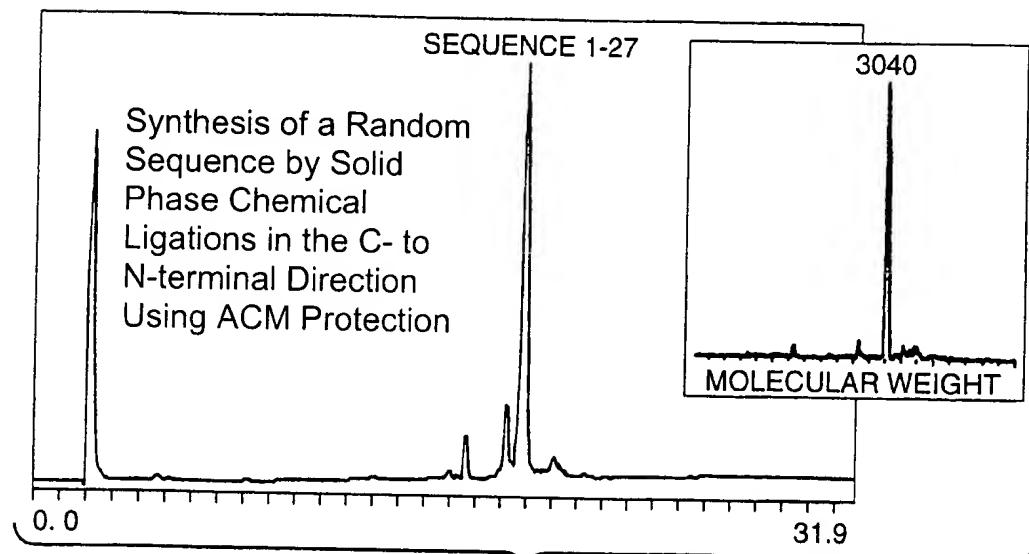
**FIG.\_27**

**ALTKYGFYGCYGRLEEKGCADRKNILA**  
1 10 19 27

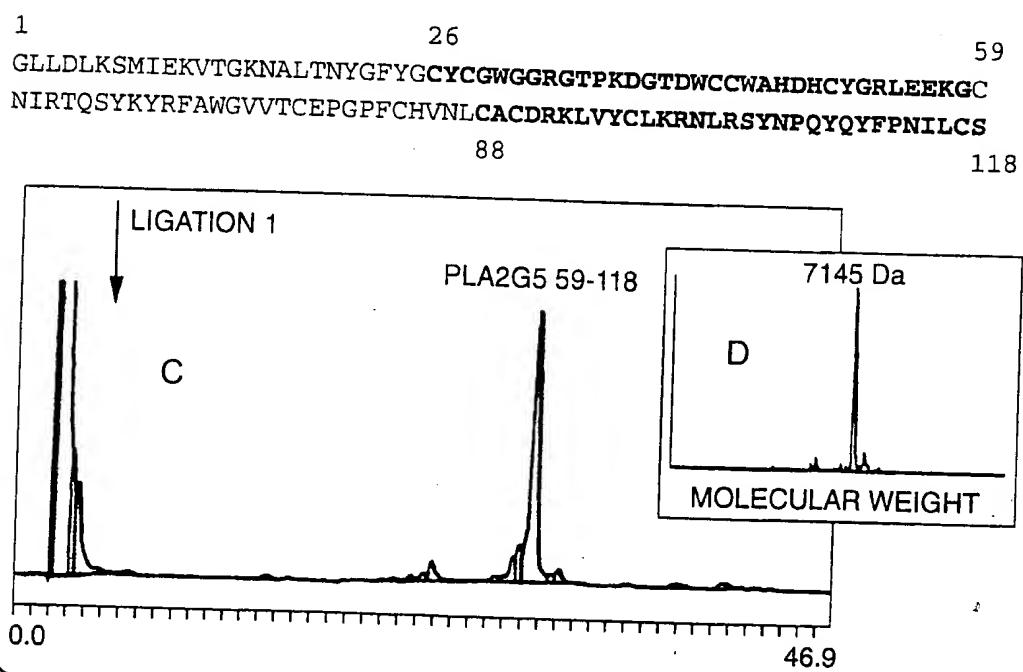
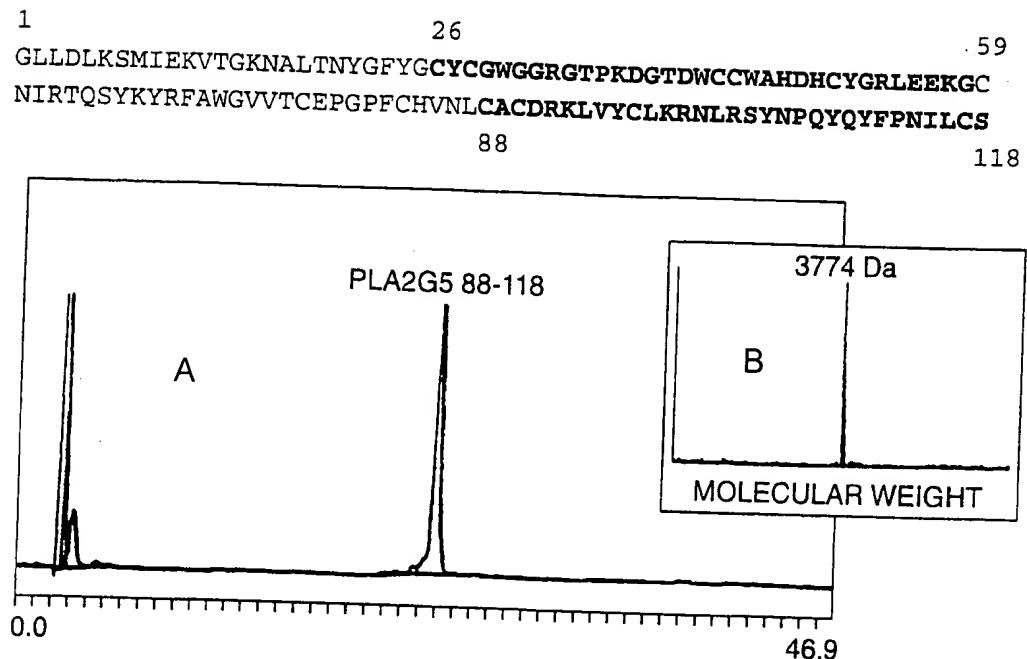


**FIG.\_28**

**ALTKYGFYGCYGRLEEKGCADRKNILA**  
1 10 19 27



**FIG.\_29**



**FIG.\_30**

FIG. 30

